Purpose of Study It is the second decade of controversy regarding the cardiovascular (CV) effects of cyclooxygenase-2 (COX-2) inhibitors. COX-2 inhibitors possess anti-inflammatory and analgesic effects comparable with conventional non-steroidal anti-inflammatory drugs, but produce fewer gastrointestinal adverse effects. Here we demonstrate that only selective COX-2 inhibitors cause disruption of the delicate balance between cholesterol efflux and influx that leads to lipid overload and macrophage foam cell formation (FCF).

Methods Used THP-1 human macrophages were incubated with: celecoxib (10 μM, 25 μM); rofecoxib (10 μM, 25 μM); naproxen (10 μM, 25 μM); acetaminophen (0.5 mM, 1 mM); oxidized low density lipoprotein (oxLDL, 25 μg/ml, 48 h) or 5 μg/ml (Dil)-oxLDL. FCF (%) oil red O stained cells) and oxLDL accumulation were determined (fluorescent intensity). Scavenger receptors: CD36, LOX-1, SR-A1 and CXCL16 and cholesterol efflux proteins: ATP-binding cassette transporter (ABC) A1 and ABCG1 were detected in macrophages by QRT-PCR and immunocytochemistry.

Summary of Results Celecoxib decreased ABCA1 and ABCG1 message in a concentration dependent manner: 68.2 ±13.36% for ABCA1 and 65.7±13.36% for ABCG1 (control set at 100%, n=6, P<0.01). Neither naproxen nor acetaminophen significantly affected expression of cholesterol efflux proteins. Both specific and nonspecific COX-2 inhibitors had a significant impact on expression of scavenger receptors CD36, LOX-1 and SR-A1—nearly double control (n=6, P<0.05). However, only specific COX-2 inhibitors significantly increased FCF in THP-1 differentiated macrophages (62.2±5.2% for celecoxib and 56.3±3.4% for rofecoxib vs. 33.5±5.1% for untreated cells, P<0.05).

Conclusions Here we report that only specific COX-2 inhibitors might contribute to atherogenesis by promoting lipid overload and lipoprotein accumulation. This may explain, in part, the increased CV risk in patients taking COX-2 inhibitors for extended periods. Despite increased scavenger receptor expression, naproxen and acetaminophen do not impact lipid content, perhaps because efflux pathways remain intact.
Purpose of Study Age-associated chronic diseases are associated with a pro-inflammatory state. It has been challenging to determine cause and effect – do age-associated pathologies increase inflammation or does inflammation induce age-associated pathologies or both? We previously showed that disease-related regenerative asynchrony in repairing lung is the cause of chronic inflammation and fibrosis. Thus, we hypothesized that the aged lung is itself asynchronously regenerating leading to a pro-inflammatory pulmonary milieu.

Methods Used Tracheas and intra-cardiac blood were harvested from C57BL6 mice in two age groups of both genders. Young mice were between 8 and 20 weeks of age. Aged mice were between 23 and 33 months of age. Tracheal epithelial progenitor cells were isolated and cultured for 6 days with continuous exposure to BrdU. Cellular regeneration was analyzed by flow cytometry for 7-AAD DNA staining in BrdU+ cells. Concentrations of an initial screening set of cytokines in plasma and cell culture supernatants from days 2 and 6 of culture were measured using magnetic bead-based assays.

Summary of Results Fewer airway epithelial progenitors underwent mitosis from the aged than the young mice (16.9±10.4% vs. 62.2±9.4% of the cultured cells at 6 days). The tracheal epithelial progenitors from aged mice were asynchronously distributed along the cell cycle (G1, S, G2/M: 44, 25, and 31%) compared to those from young mice (62, 14, and 24%). Plasma concentrations of IL-1β, IL-6, TNFα and TGFβ were not significantly different between age groups. Concentrations of TGFβ were significantly different between age groups in supernatant from day 2 (aged=112.43±16.31 pg/mL, young=171.23 ±13.70 pg/mL; p<0.05) but not from day 6 of culture (aged=159.60±29.83 pg/mL, young=214.15±.94 pg/mL; p=NS). Concentrations of IL-1β were not significantly different between age groups in supernatant from day 2 of culture (aged=2.01±0.23 pg/mL, young=2.10±0.24 pg/ mL; p=NS) but remained higher in aged compared to young progenitors on day 6 (aged: 2.17±0.31 pg/mL, young: 1.26±0.10 pg/mL; p<0.05).

Conclusions Our data support the concept that aging induces progenitor cell mitotic asynchrony. It is possible that this epithelial mitotic asynchrony contributes to the pro-inflammatory state associated with aging, as seen in other chronic inflammatory states.

Desmopressin (DDAVP) has been used to raise the serum levels of vWF in these patients. However, not all patients with Type 1 vWD are known to respond to DDAVP therapy. We sought to compare the levels Factor VIII, vWF antigen, ristocetin and fibrinogen at different time points to determine the single most useful time point for ascertaining the patient as a responder.

Methods Used Levels of Factor VIII, vWF antigen, ristocetin and fibrinogen has been conventionally measured at multiple time points after a DDAVP challenge. We conducted a retrospective analysis on 89 patients who received the DDAVP challenge test and compared their factor levels at 0, 30, 60, 90 and 120 minutes.

Summary of Results Levels of Factor VIII, vWF antigen ristocetin and fibrinogen were significantly elevated (p<0.001) at 30, 60, 90 and 120 minute time points when compared to their baseline values. A downturn was noted for Factor VIII, vWF antigen and ristocetin levels at the 90 minute time point but fibrinogen levels did not significantly change compared to the baseline level.

Conclusions In this study we show that measurement of factor levels at any one time point, preferably at 60 minutes is sufficient to diagnose a patient as a responder after a DDAVP challenge test. Curtailling the number of time points measurement will result in significant savings in cost and time to patients and their providers.

Purpose of Study More than 100,000 pelvic surgeries to remove ovarian masses (BOM) are performed yearly in the USA only 8% of those remove ovarian cancer. Circulating microRNA are biomarkers for disease detection. Purpose of study: 1. To analyze patterns of microRNAs in women with BOM and OvCa 2. Discover pathway involved malignant transformation.

Methods Used Plasma from 32 women OvCa, 24 controls (BOM) was analyzed using ABI Taqman OpenArray MicroRNA pools A and B to measure the expression of 754 known miRNAs .Real-time PCR was performed on the Taqman Open Array MicroRNA arrays using the Applied Biosystem Open Array Real-Time PCR system. Data were unable to be published.
processed using the OpenArray Real-Time qPCR analysis software and exported for analysis using the Applied Biosystems DataAssist Software. Data analysis was done with the R programming language. A cutoff for Ct values at 30 was used. MiRNAs with Ct values higher than 30 were considered not detected. Data was normalized using a mean-centering restricted (MCR), a modification of the traditional delta Ct method and uses miRNAs which are expressed in all samples for data normalization. Statistical analysis was performed via custom scripts based on the R/Bioc conductor package LIMMA (Linear Models for Microarray).

**Summary of Results** BOM had higher expression (2-14 fold higher) of miRs −195, −126, −139-5p, −27b, −127, −152, −28, −106b, −17, −363, −181a, −192 relative to OvCa (p<0.0006). OvCa over-expressed of miRs −1274a, −720 and −625-3p (p<0.0007). Reactome pathway analysis detected involvement of miRs into pathways of activation of BAD, PI3/AKT signaling in CD28 and activation of BH3 in BOM these pathways were not detected in OvCa (p<0.000596).

**Conclusions** BOM patients have immune recognition and pro-apoptotic protective circulating microRNAs. It is unknown whether miRs originate in ovary or another tissue. Recent work shows that BH3 mimetics are very effective in inducing cancer cell death.

**IMPACT OF LATE USE MAGNESIUM SULFATE IN INNER CITY CHILDREN HOSPITALIZED FOR ASTHMA EXACERBATION**

P Shukla, E Aragona, J Wang, D Pillai. Division of Pulmonary and Sleep Medicine, Children’s National Medical Center, Washington, DC, United States

10.1136/jim-2016-000080.8

**Purpose of Study** Asthma is typically treated acutely with β2-agonists and systemic steroids. Adjunctive therapies such as magnesium sulfate (MgSO4) have proven useful with early addition potentially improving clinical outcomes in asthma (reduced hospital admission rates, length of stay and intubation rates). Exact administration time and impact on outcomes in children are not fully understood. We sought to identify the impact of timing of initiating MgSO4 therapy in innercity children admitted for status asthmaticus.

**Methods Used** We performed a retrospective chart review of children (age 2–21 yrs) admitted to a children’s hospital over a 12 month period with asthma exacerbation and administered MgSO4. Data collected included ethnicity, gender, medications, timing of interventions, length of stay, BMI percentile, comorbidities and NAEPF asthma severity. Statistical analysis performed with SPSS 22.

**Summary of Results** 150 innercity children were admitted for asthma exacerbation and received MgSO4 during the study period. 85% were African American, 36% female, 39% had moderate/severe asthma and mean time to initial MgSO4 was 3.8 hours from triage. Those receiving initial MgSO4 after 4 hours were more likely to receive multiple doses of MgSO4 (OR2.8 [95%CI:1.4–5.6]). Time of initial MgSO4 dose (<4 vs. >4 hrs) showed no significant difference in other parameters including age, obesity, asthma severity, and comorbidities. A sub-analysis of children that received 1 dose vs. >1 MgSO4 dose demonstrated that those receiving >1 MgSO4 doses were more likely to be obese (OR2.7 [1.3–5.7]), have moderate/severe asthma (OR3.2 [1.6–6.8]) and have increased length of stay (p=0.005) and charges (p=0.042). Additionally, obese children (OR8.9 [2.2–35.2]), and intermittently/mild asthmatic children (OR6.4 [1.2–31.2]) receiving >1 MgSO4 dose were more likely to have >2 day length of stay.

**Conclusions** Delay in administration of MgSO4 in children hospitalized for status asthmatics may be associated with poor outcomes including multiple doses of MgSO4 which in turn is associated with longer length of stay and increased charges. Obesity and asthma severity are important factors associated with these outcomes. A prospective analysis in a larger cohort is recommended to further evaluate these findings.

**AN IN VIVO MODEL OF HUMAN AIRWAYS FOR INVESTIGATING FIBROSIS**

S Ferrante,1 T Hackett,2 C Hoptay,1 J Engelhardt,3 J Ingram,4 Y Zhang,3 S Alcala,1 F Shaheen,2 E Matz,1 D Pillai,1 R Freishtat1, 1Children’s National Medical Center, Washington, DC, United States; 2Centre for Heart Lung Innovation, St Paul’s Hospital, Vancouver, BC, Canada; 3University of Iowa, Iowa City, IA, United States; 4Duke University, Durham, NC, United States

10.1136/jim-2016-000080.9

**Purpose of Study** Limited models exist to investigate the airway epithelium’s role in repair, regeneration, and pathology of chronic obstructive lung diseases. We introduce a human asthmatic airway epithelial xenograft system integrating a proliferating and differentiating airway epithelium with an actively remodeling rodent mesenchyme in an immunocompromised murine host. We hypothesized that epithelial regeneration in asthma induces underlying matrix fibrosis.

**Methods Used** Human airway epithelial cells from asthmatic and non-asthmatic donors (n=5 per group) were seeded into decellularized rat tracheas. Tracheas were ligated to a sterile tubing cassette and implanted subcutaneously in the flanks of athymic nude mice. Grafts were harvested at 2, 4, or 6 weeks for analysis of tissue histology, fibrillar collagen deposition, and TGFβ1 activation. Non-transplantable human lungs from asthmatic and non-asthmatic donors FFPE sections were analyzed using similar methods.

**Summary of Results** Grafted epithelial cells generated a differentiated epithelium with basal, ciliated, and mucus cells. By 4 weeks post-engraftment, asthmatic-derived epithelium showed decreased numbers of ciliated cells and E-cadherin expression compared to non-asthmatic controls, similar to human lung biopsy tissue. 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 epithelial seeded grafts. This was accompanied by a >2-fold induction of matrix TGFβ1 [with evidence of pSMAD3 activity] in asthmatic grafts at 4
Summary of Results

LDL).

ger receptor with the capacity to endocytose oxidized could compromise macrophage clearance of lipids, also observed. In CKD, a paradoxical decrease in CD36 formation to lowering of ABCA1, augmentation of CD36 was

fi

pro-atherogenic suppression of ABCA1, differs from our lack of response to statins. This mechanism, through explain the pathogenesis of elevated CVD risk in CKD and may

Conclusions

control.

phages exposed to CKD plasma as compared to healthy mRNA was decreased by 36±7% (p<0.0001) in macro-

mRNA was reduced by 23±5% (p<0.0001) while CD36 mRNA was reduced by 23±5% (p<0.0001) while CD36

 incubation for 18 h

(ABC)A1 (cholesterol ef

fl

PCR analysis showed that ABCA1 mRNA was reduced by 46.45±3.4% and 50.27±8.9% (P<0.01), respectively . Following 18 h incubation in

ABC2G1 expression increased by 58.42±6.32% and 65.45±5.24% vs. control (P<0.01), respectively . ABCG1 expression

increased by 58.42±6.32% and 65.45±5.24% vs. control

increasing vulnerability to lipoprotein thrombi in kidney. Further lowering of monocyte CD36 with statins would be of little benefit if CD36 is already low in CKD. Defining changes in lipid handling in CKD could lead to novel, targeted CVD treatment approaches in the CKD population.

Conclusions

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.

Purpose of Study

Chronic kidney disease (CKD) is a known risk factor for cardiovascular disease (CVD). Patients with CKD have a high prevalence of atherosclerosis. However, CVD risk associated with CKD is not entirely explained by standard lipid profile or liver handling of cholesterol, as evidenced by the resistance to statin benefits seen in later stages of CKD. This study aims to detect changes in expression of cholesterol transport proteins in the setting of CKD and to determine if such changes adversely affect lipid handling by macrophages leading to cholesterol overload and atheromatous foam cell formation.

Methods Used

THP-1 human macrophages were incubated for 18 h–24 h with plasma obtained from 10 CKD patients (7 male, 3 female) or 10 healthy control subjects (4 male, 6 female). CKD patients were not on dialysis and had not received renal transplant. Following incubation, mRNA was isolated and reverse transcribed. The resulting cDNA was subjected to quantitative real-time PCR using specific primers for ATP binding cassette transporter (ABCA1 and ABCG1, liver X receptor (LXR) and cholesterol esterol transport via upregulation of cholesterol efflux proteins ATP-binding cassette transporter (ABCA1 and ABCG1, liver X receptor (LXR) and cholesterol 27-hydroxylase. MTX is non-specific and associated with adverse effects on liver and kidney. Therefore, this study examines the anti-atherogenic efficacy of a specific A2aR agonist, UK-432,097, a drug with an established safety profile in humans.

Methods

Used

Purpose of Study

Chronic kidney disease (CKD) is a known risk factor for cardiovascular disease (CVD). Patients with CKD have a high prevalence of atherosclerosis. However, CVD risk associated with CKD is not entirely explained by standard lipid profile or liver handling of cholesterol, as evidenced by the resistance to statin benefits seen in later stages of CKD. This study aims to detect changes in expression of cholesterol transport proteins in the setting of CKD and to determine if such changes adversely affect lipid handling by macrophages leading to cholesterol overload and atheromatous foam cell formation.

Methods

Used

THP-1 human macrophages were incubated for 18 h–24 h with plasma obtained from 10 CKD patients (7 male, 3 female) or 10 healthy control subjects (4 male, 6 female). CKD patients were not on dialysis and had not received renal transplant. Following incubation, mRNA was isolated and reverse transcribed. The resulting cDNA was subjected to quantitative real-time PCR using specific primers for ATP binding cassette transporter (ABCA1 and ABCG1, liver X receptor (LXR) and cholesterol 27-hydroxylase. MTX is non-specific and associated with adverse effects on liver and kidney. Therefore, this study examines the anti-atherogenic efficacy of a specific A2aR agonist, UK-432,097, a drug with an established safety profile in humans.

Methods

Used

Purpose of Study

Chronic kidney disease (CKD) is a known risk factor for cardiovascular disease (CVD). Patients with CKD have a high prevalence of atherosclerosis. However, CVD risk associated with CKD is not entirely explained by standard lipid profile or liver handling of cholesterol, as evidenced by the resistance to statin benefits seen in later stages of CKD. This study aims to detect changes in expression of cholesterol transport proteins in the setting of CKD and to determine if such changes adversely affect lipid handling by macrophages leading to cholesterol overload and atheromatous foam cell formation.

Methods

Used

Purpose of Study

Chronic kidney disease (CKD) is a known risk factor for cardiovascular disease (CVD). Patients with CKD have a high prevalence of atherosclerosis. However, CVD risk associated with CKD is not entirely explained by standard lipid profile or liver handling of cholesterol, as evidenced by the resistance to statin benefits seen in later stages of CKD. This study aims to detect changes in expression of cholesterol transport proteins in the setting of CKD and to determine if such changes adversely affect lipid handling by macrophages leading to cholesterol overload and atheromatous foam cell formation.

Methods

Used
Purpose of Study

Studies have linked the use of anti-secretory agents to nosocomial complications including Clostridium difficile–induced pseudomembranous colitis and hospital acquired pneumonia. Although there are comprehensive evidence-based guidelines for the initiation of stress ulcer prophylaxis, there is still a universal acceptance of these agents, despite nationwide disorganization in current practice, which has led to their overuse. While many studies have shown the perversiveness of stress ulcer prophylaxis overuse in the hospital setting, none have demonstrated its effect on the community through the improper discharge of patients on these medications.

Methods Used

A retrospective review of patient data at a major teaching hospital in New York City was performed. During a 2 month study period, adult non-intensive care patients were randomly selected to determine the incidence of inappropriate initiation of stress ulcer prophylaxis on admission, as compared to the incidence of appropriate use. A follow-up assessment was then completed to determine the incidence of patients that were inappropriately discharged on these medications.

Summary of Results

A total of 100 randomly selected patients throughout the inpatient medicine service were analyzed. The results showed a high rate of inappropriate initiation and discharge of patients on anti-secretory agents. The study showed a 50% (n=50) incidence of overall stress ulcer prophylaxis use. Of the patients on stress ulcer prophylaxis, a 76% (n=38) incidence of inappropriate use was found. Of the patients inappropriately discharged on stress ulcer prophylaxis, there was a 53% (n=19) incidence of inappropriate discharge home on these medications.

Conclusions

This study highlights the continued inappropriate initiation and discharge of patients on anti-secretory agents, despite mounting evidence and advisories against this practice. The use of an electronic medical record could provide an additional resource to improve quality of care. Electronic prescriptions allow for prompts that ask for a clinical indication during the prescription process. The advent of this technology may yield even more promising improvements in clinical practice, and its implementation is the current focus of a continuing study.

Moderated Poster

11:45 PM – 1:05 PM

Wednesday, April 13, 2016

MP1

CORRECTING Atherogenic EFFECTS of Lupus Plasma on Macrophages with Resveratrol and Mycophenolate

NM Siegert,1,2 L Voloshyna,1 J DeLeon,2 SE Carsons,2,1 I Teboul,1,2 LJ Kasselman,1,2 J Mattana,2 AB Reiss1,2 1Winthrop Research Institute, Winthrop-University Hospital, Mineola, NY, United States; 2Medicine, Winthrop-University Hospital, Mineola, NY, United States

Purpose of Study
Premature atherosclerosis with coronary artery disease is a major cause of morbidity in Systemic Lupus Erythematosus (SLE). SLE patient plasma induces a pro-atherogenic profile of cholesterol transport genes in macrophages. A common immunosuppressive treatment for SLE, mycophenolate (MMF) reduces scavenger receptors thus reducing lipid influx. We have demonstrated atheroprotective properties of the polyphenol resveratrol on cholesterol efflux. This study determines whether MMF and resveratrol work synergistically to regulate cholesterol transport in macrophages exposed to pro-atherogenic SLE plasma.

Methods Used

THP-1 human macrophages (105/ml) were incubated in 10% SLE plasma with: media (control); MMF (1 μg/ml); resveratrol (50 μM); and MMF+resveratrol. After 24 h incubation, total RNA and protein were isolated. Message level of scavenger receptors CD36, LOX1, and SRA1; and efflux proteins 27-hydroxylase, ATP binding cassette transporter (ABC)A1, and ABCG1 were evaluated by QRT-PCR and confirmed by immunoblot. Cholesterol efflux was measured by Amplex Red Cholesterol Assay kit run ± cholesterol esterase.

Summary of Results

In 10% SLE plasma, MMF suppressed efflux genes ABCA1 and ABCG1 (58.38±3.5% and 72.98±3.3%) vs. SLE plasma alone (p<0.0001) while MMF+resveratrol corrected this suppression. In SLE plasma, MMF+resveratrol decreased ScrA1 and LOX-1 by 15±2.5% and 47±1.0%, respectively vs. resveratrol alone (p<0.0001). SLE plasma promoted cholesterol accumulation in THP-1 macrophages and prevented efflux into medium. It increased the ratio of cholesterol esters to free cholesterol (ChE/FC). Resveratrol decreased intracellular cholesterol and restored ChE/FC ratios to that of cells in healthy control plasma.

Conclusions

MMF and resveratrol exhibit complimentary effects on macrophages exposed to SLE plasma. Both agents combined restore cholesterol influx and efflux gene expression to that of cells treated with control plasma.
Resveratrol additionally reverses cholesterol accumulation caused by SLE plasma. Further evaluation of resveratrol + MMF in atherosclerosis in SLE may lead to improved treatment.

**Abstract MP2**

**PATHOPHYSIOLOGY AND METABOLIC PHENOTYPE OF LOW BODY MASS INDEX DIABETES**

A Tiwari,1 RD Gupta,7 S Kehlenbrink,1 M Carey,1 V Padmanaban,2 N Thomas,2 M Hawkins1. 1Endocrinology, Albert Einstein College of Medicine, Bronx, NY, United States; 2Endocrinology, Christian Medical College, Vellore, India

**Purpose of Study** Millions of individuals with low body mass index (BMI) globally have diabetes of unclear etiology. These include patients with Fibrocalculous Pancreatic Diabetes (FCPD) and Lean Diabetes (LD), defined by the presence or absence of pancreatic calcifications on ultrasound. We present the first studies using gold-standard methodologies to assess their metabolic phenotype.

**Methods Used** Stepped euglycemic-hyperinsulinemic (∼30 and 80 mU/m²/min) clamp studies were performed in n=8 Indian males with LD (age 38±3 y, BMI 18.4±0.1 kg/m², HbA1c 11.0±0.8%) and n=22 with FCPD (age 30±1 y, BMI 19.7±0.6 kg/m², HbA1c 10.2±0.6%), compared with n=12 type 2 diabetes subjects (T2DM, BMI 25.7±0.3 kg/m², HbA1c 9.7±0.6%) and n=12 age and BMI matched non-diabetic (ND) subjects and n=16 with type 1 diabetes (T1DM, HbA1c 9.1±0.3%). Therapeutic regimens were intensified for two weeks to correct glucose toxicity in all groups. Lean body mass was determined for all subjects from percentage of total body fat as assessed by DXA.

**Summary of Results** Peripheral insulin sensitivity (Rd, mg/kg lean body weight/min), was markedly impaired in T2DM (2.3±0.6; p<0.01) compared to LD (9.2±1.6) and FCPD (5.8±0.7). Rd did not differ between T1DM (5.8±0.7), LD and FCPD groups (figure 1).

**Conclusions** Thus, these comprehensive studies suggest patients with LD and FCPD are only mildly insulin resistant once hyperglycemia is corrected. This promotes a paradigm shift in our understanding of low body mass index diabetes and could have profound therapeutic implications for millions of people.

**Abstract MP3**

**ROLE OF HISTONE DEACETYLASE (HDAC) INHIBITORS IN ADULT T-CELL LYMPHOMA/LEUKEMIA (ATL)**

N Mukhi, G Sidhu, J Gonsky, I Shapira. Hematology/oncology, SUNY Downstate Medical Center, Glen Oaks, NY, United States

**Purpose of Study** ATL is a peripheral T-cell neoplasm (PTCL) associated with human T-cell lymphotropic virus-1 (HTLV-1) infection. Currently there is no established therapy for relapsed/refractory disease. Initial in-vitro studies of HDAC inhibitors showed selective apoptosis of HTLV-1 infected T cell lines. In phase II trial for relapsed/refractory PTCL, 2 patients had EBV and 1 patient had HBV reactivation. It was unclear if this was from HDAC induced immunosuppression or direct promotion of viral replication or underlying disease process. All HDAC inhibitors trials in last 6 years excluded ATL patients although they are approved for this disease. We here describe our experience of 3 patients with relapsed/refractory ATL treated with HDAC inhibitor romidepsin.

**Methods Used** Chart review of patients with relapsed/refractory ATL treated with romidepsin at King’s County Hospital.

**Summary of Results** Case 1: 43 year old male with acute ATL who progressed on EPOCH after 4 cycles. Romidepsin was started at 14 mg/m² IV Day 1, 8, 15 Q28 days. He tolerated cycle 1 well but continued to have progressive disease. Patient died 40 days after initiation of therapy from infection.

Case 2: 37 year old male with acute ATL who had disease progression on EPOCH×2 cycles. He was started on romidepsin 10 mg/m² IV (dose reduced due to T. bili 3.5 gm/dl). After first dose, his platelets dropped to 20 k/mm³ necessitating treatment delay and dose reduction to 6 mg/m². He had temporary response as evidenced by reduction in WBC count from 103 k/mm³ to 5 k/mm³ and improvement in liver function. He only received 1 dose and died on Day 50 from disease progression.

Case 3: 47 year old male with ATL lymphoma initially treated with CHOP×6 cycles and relapsed after 1 year with peripheral lymphocytosis to 57 k/mm³ and diffuse lymphadenopathy. He received ICE×2 cycles with progressive disease. He was started on romidepsin 14 mg/m². He received 1 dose and had Grade IV anemia/thrombocytopenia. He developed urosepsis and expired on Day 20.

**Conclusions** In our small experience of romidepsin in relapsed/refractory ATL, patients appear to have modest response rates and higher rate of cytopenias when compared to other PTCL subtypes in clinical trials. Given the concerns for viral reactivation and lack of data for use of romidepsin in ATL, it should be used cautiously.
Abstracts

MP4 MICROCYTOSIS IN PERNICIOUS ANEMIA WITHOUT IRON DEFICIENCY OR THALASSEMIA TRAIT

M Sajani, P Draksharam, S Atrona, AS Braverman. Hematology/Oncology, SUNY Downstate Medical Center, Brooklyn, NY, United States

10.1136/jim-2016-000080.16

Purpose of Study To demonstrate the presence and attributes of microcytes in Pernicious Anemia (PA) patients with high Red blood cell (RBC) distribution widths (RDW), but without iron deficiency or thalassemia trait. Marked microcytosis is typical of PA, but their RDW are usually elevated (>21%).

Methods Used Cases and Methods We report two patients with severe anemia, B12 deficiency, and elevated RDW’s.

Patient 1: 55 y/o African-American man, with dyspnea, finger paresthesia without gait disturbance. WBC 2.4 K/ul, Hb 4.8 g/dl, MCV 84.8 fl, RDW 30%, reticulocyte count 15 K/ul, iron 234 µg/dl, ferritin 880 µg/dl, platelets 70 K/ul, LDH 5980 U/L, B12 <30 pg/ml.

Patient 2: 37 y/o African-American woman with long hx of anemia, recent weakness, and gait disturbance. WBC 3.5, Hb 6.3, MCV 114, RDW 29.5%, reticulocyte count 27, iron 108, TIBC 304 mg/dl, ferritin 50, platelets 45, LDH 2484, B12 60.

Both patients’ hematologic parameters normalized within 1–7 months after B12 treatment.

Summary of Results Microcytes constituted 32.8% of 1000 RBC in patient 1, whose MCV was normal, and 19.3% in patient 2. They were minute, irregular or twisted cells, often with two very unequal dimensions. They were often normochromic, or even hypochromic. Twenty of the small cells were present, which were their smallest dimension ranged from 2–4 microns, with an average of 3.0 microns. The larger dimension averaged 1.5–2.0 times greater than the smaller. The larger cells were circular or elliptical, with equal dimensions ranging from 6.2 to 13 microns.

Conclusions Although the coexistence of macrocytic and normocytic RBC may help to explain PA patients’ high RDW, a significant percentage of their RBC may be microcytic. These microcytes are smaller than those in iron deficiency or thalassemia, have very irregular shapes (micro-poikilocytes), and resemble neither other types of microcytes nor schistocytes. The microcytes in one patient reduced his MCV to a normal level. These microcytes may be the result of megaloblastic dyserythropoiesis.

MP5 STABLE ISOTOPE LABELED BY AMINO ACID IN CULTURE (SILAC) STRATEGY TO ANALYZE HUMAN MIDDLE EAR EPITHELIAL CELLS (HMEEC) SECRETOME IN RESPONSE TO NTHI LYSATES: EVIDENCE OF THE IMPLICATION OF EXOSOMES IN OTITIS MEDIA

S Val,1 S Jeong,1 M Foley,1 A Krueger,1 G Nino,2 K Brown,2 D Preciado1,1
1Sheikh Zayed Institute, Children’s National Medical Center, Washington, DC, United States; 2Center for Genetic Medicine, Children’s National Medical Center, Washington, DC, United States

10.1136/jim-2016-000080.17

Purpose of Study This study aimed at characterizing the secretome of HMEEC-1 and to evaluate its regulation in response to NTHi lysates and better understand the pathogenesis of Otitis Media (OM).

Methods Used HMEEC-1 were labeled with heavy isotopes of arginine and lysine to obtain a spike-in standard that was mixed with the conditions of interest (control or treated 24 hrs, secretions recovered 24 hrs or 48 hrs) and separated by SDS-PAGE. Peptides generated by in-gel digestion were analyzed by LC-MS/MS. Middle ear effusions (MEEs) from patients having chronic OM were analyzed to validate the results obtained with HMEEC.

Summary of Results 767 proteins were detected by MS in HMEEC secretions. The more abundant proteins detected were components of the extracellular matrix, proteins implicated in the innate immune response, and surprisingly proteins implicated in the processing and packaging of RNA. These proteins were heterogenous nuclear ribonucleoproteins A2/B1 (hnRNPA2B1) and K (hnRNPK) enriched at the 24 hrs time point (1.99 and 1.78 fold change respectively) and Q at 48 hrs (hnRNQ, fold change 4.76) in response to NTHi lysates. We then hypothesized that these proteins were implicated in the packaging of miRNAs in exosomes in response to NTHi lysates. An exosome marker assay showed the presence of exosomes in both the cell secretions and MEEs. A western blot analysis of MEE exosome proteins showed the presence of hnRNPs as in cell secretions. Finally, a Nanostring chip assay demonstrated the presence of 8 miRNA in MEEs, mostly reported to be produced by epithelial cells and neutrophils.

Conclusions We characterized the secretome of HMEEC in response to NTHi lysates treatment that show a potential implication of exosomes in the pathogenesis of OM. We demonstrated the presence of exosomes in HMEEC secretions and MEEs, transporting miRNAs packaged by hnRNPs proteins.

MP6 HOMOCYSTEINE LEVEL IN PFO RELATED STROKE PATIENTS WITH RESPECT TO MEDICAL THERAPY VS PFO CLOSURE

W Deng, T Wilcham, D McMullin, K Feeney, S Silverman, I Inglessis, I Palacios, EH Lo, FS Buonanno, M Ning. Neurology, Massachusetts General Hospital, Boston, MA, United States

10.1136/jim-2016-000080.18

Purpose of Study Homocysteine is an independent risk factor of ischemic stroke by promoting vascular endothelial dysfunction and thrombotic process through oxidative stress. We previously found that PFO closure may reduce total homocysteine level (tHcy) in plasma. Here, we compare the effect of PFO closure and medical treatment in reducing mild homocysteinemia in PFO-related stroke patients.

Methods Used 28 PFO-related stroke patients with mildly elevated tHcy (>12 µmol/l) were prospectively recruited in accordance with IRB. 14 received PFO closure and 14 were treated by medical therapy (antiplatelet/anticoagulant) alone. None of the patients were on folate or vitamin B
supplementation. Plasma was collected at baseline and 1 year follow-up after treatment. tHcy level was determined by selected reaction monitoring using mass spectrometry.

**Summary of Results** Compared to medical therapy, PFO closure resulted in a lower tHcy level during follow-up (PFO closure: 11.13±3.94 μmol/L, medical therapy: 15.48 ±3.55 μmol/L, p=0.006), with no difference at baseline (PFO closure: 17.77±4.39 μmol/L, medical therapy: 16.47 ±7.50 μmol/L, p=0.575). Mild hyperhomocysteinemia patients post PFO closure had a significant reduction of tHcy by 37.34% (p=0.0005), with 71.43% of the patients (PFO closure: 17.77±4.39 mol/L, medical therapy: 16.47 ±7.50 mol/L, p=0.006). No difference at baseline (PFO closure: 17.77±4.39 μmol/L, medical therapy: 16.47 ±7.50 μmol/L, p=0.006), with no difference at baseline (PFO closure: 17.77±4.39 μmol/L, medical therapy: 16.47 ±7.50 μmol/L, p=0.006). Milder hyperhomocysteinemia may be important for future thrombotic risk. Understanding the mechanism of PFO-related tHcy changes is important in optimizing medical treatment (e.g., folate replacement); studies are ongoing.

**Abstract MP6 Figure 1**

**Purpose of Study** To determine whether genetic rather than environmental factors may be responsible for the occurrence of these neoplasms in families.

**Methods Used** We interrogated our registry of >700 pedigrees of families (fams) with multiple hematologic malignancies. We identified 31 families with both NHL and MM in their pedigrees. In 16 pedigrees a parent and child were affected (12 father-child pairs and 4 mother-child pairs). Fifteen affected sib pairs were identified in the 31 fams, 10 same sex pairs and 5 male-female pairs. Six of the 31 pedigrees had only 1 affected pair. More distant relationships were observed in other fams.

**Summary of Results** Male transmission was evident in 25 fams and female transmission was observed in 6. NHL and MM cases had at least 1 unaffected generation (gen) between them in 8 pedigrees, and the diseases occurred in sequential (13 fams) or the same gen in 10 fams. MM was the diagnosis (dx) in the youngest affected gen in 9 pedigrees, NHL in 13 pedigrees and both occurred in the youngest gen in 9 fams. The median age at dx of 29 NHL patients for whom data were available was 55 yrs (range, 20–99 yrs), and the median age at dx of 26 MM cases was 56 yrs (range, 30–82 yrs). Ten of 26 MM patients were <50 years old at dx. The presence or absence of anticipation could be assessed in 15 of the 31 pedigrees. All 15 displayed anticipation in terms of succeeding gens developing NHL or MM at an earlier age than did the previous gens (median ~19 yrs, range ~6 to ~56 yrs).

**Conclusions** We demonstrate anticipation in 15 assessible fams with both NHL and MM, a feature of familial MM that we previously reported (Despande HA, et al: Br J Haematol 1998). More advanced, aggressive disease at dx in the youngest gen is another feature of anticipation, and was observed in 9 of 13 fams in which it could be assessed. Demonstration of anticipation in all 15 evaluable fams suggests a genetic basis for the relationship between these two B-cell disorders. The increase of same sex sib pairs among affected sib pairs implicates a locus on a pseudo-autosomal region of the X chromosome as potentially responsible for this observation, as we have previously reported for Hodgkin’s lymphoma (Horwitz M, Wiernik PH, Am J Hum Genet 1999). Myeloma and non-Hodgkin’s lymphoma may have common genetic causation; molecular studies of these fams are planned.

**MP7 FAMILY WITH BOTH NON-HODGKIN’S LYMPHOMA (NHL) AND MYELOMA (MM): ANTICIPATION AND MALE TRANSMISSION**

PH Wiernik, JP Dutcher. Cancer Research Foundation, Chappaqua, NY, United States

**Purpose of Study** To determine whether genetic rather than environmental factors may be responsible for the occurrence of these neoplasms in families.

**Methods Used** We interrogated our registry of >700 pedigrees of families (fams) with multiple hematologic malignancies. We identified 31 fams with both NHL and MM in their pedigrees. In 16 pedigrees a parent and child were affected (12 father-child pairs and 4 mother-child pairs). Fifteen affected sib pairs were identified in the 31 fams, 10 same sex pairs and 5 male-female pairs. Six of the 31 pedigrees had only 1 affected pair. More distant relationships were observed in other fams.

**Summary of Results** Male transmission was evident in 25 fams and female transmission was observed in 6. NHL and MM cases had at least 1 unaffected generation (gen) between them in 8 pedigrees, and the diseases occurred in sequential (13 fams) or the same gen in 10 fams. MM was the diagnosis (dx) in the youngest affected gen in 9 pedigrees, NHL in 13 pedigrees and both occurred in the youngest gen in 9 fams. The median age at dx of 29 NHL patients for whom data were available was 55 yrs (range, 20–99 yrs), and the median age at dx of 26 MM cases was 56 yrs (range, 30–82 yrs). Ten of 26 MM patients were <50 years old at dx. The presence or absence of anticipation could be assessed in 15 of the 31 pedigrees. All 15 displayed anticipation in terms of succeeding gens developing NHL or MM at an earlier age than did the previous gens (median ~19 yrs, range ~6 to ~56 yrs).

**Conclusions** We demonstrate anticipation in 15 assessible fams with both NHL and MM, a feature of familial MM that we previously reported (Despande HA, et al: Br J Haematol 1998). More advanced, aggressive disease at dx in the youngest gen is another feature of anticipation, and was observed in 9 of 13 fams in which it could be assessed. Demonstration of anticipation in all 15 evaluable fams suggests a genetic basis for the relationship between these two B-cell disorders. The increase of same sex sib pairs among affected sib pairs implicates a locus on a pseudo-autosomal region of the X chromosome as potentially responsible for this observation, as we have previously reported for Hodgkin’s lymphoma (Horwitz M, Wiernik PH, Am J Hum Genet 1999). Myeloma and non-Hodgkin’s lymphoma may have common genetic causation; molecular studies of these fams are planned.

**MP8 MONOCLONAL GAMMOPATHY CHARACTERIZATION USING SERUM PROTEIN ELECTROPHORESIS IN A MAJOR URBAN POPULATION**

DB Laskar, K Shafique, C Lu, A Zuretti. Pathology, SUNY Downstate Medical Center, Brooklyn, NY, United States

**Purpose of Study** Serum protein electrophoresis (SPEP) with subsequent immunofixation (IF) are clinical laboratory techniques used to evaluate a wide-range of disorders where abnormal serum protein quantities are characteristic (e.g., multiple myeloma (MM), MGUS, amyloidosis, HIV/AIDS, SLE, CML/NHL). Thus, it is important to identify or exclude malignancy when considering the analyses. Our aim is to characterize SPEP patients from our institution, a predominantly black population.

**Methods Used** We retrospectively reviewed 50 patient’s SPEP/IF results. Data recorded were SPEP/IF results, monoclonal immunoglobulin (Ig) identity, clinical diagnoses, age, race, and gender. Univariate analysis was used to describe patient demographics. Parametric analysis was used to compare the monoclonal gammopathy (MG) group versus non-MG group.

**Summary of Results** Age range was 12–86 years, mean age was 62 years and male to female ratio was 1:3.5. Forty-eight (96%) patients identify as black, 1 (2%) Asian
Abstract MP8 Figure 1

and 1 (2%) white. SPEP patterns showed 1 (2%) patient had acute inflammation, 3 (6%) had chronic inflammation, 24 (48%) were inconclusive, 16 (32%) had MGs, 3 (6%) had normal results and 3 (6%) had polyclonal bands (table 1). Among MG patients, IgG was most common isotype (75%), kappa was most common light chain (58%) and IgG kappa was most common (44%). Mean age was 69 years for MG patients and 58 years for non-MG patients.

MM was identified in 9 (18%) patients; 89% (8/9) had normal total protein (TP) levels and 1 (11%) had increased TP. Neuropathy was seen in 7 (14%) patients; 71% (5/7) had polyclonal gamma Ig increase, and 1 (14%) case with co-HIV infection had monoclonal IgG kappa. Seven (14%) patients had CKD, 4 (8%) had HIV/AIDS, 3 (6%) had anemia, 3 (6%) had MGUS, 1 (2%) had SLE and the remaining 16 (32%) had other co-morbidities (i.e. HTN, DM, CAD, etc.).

Conclusions SPEP/IF analyses were used to characterize 50 patients. A wide-range of disorders were observed. MG patients were 11 years older than non-MG patients. IgG kappa was most common MG. Our study showed female-predominance. This study shows SPEP utility to discern various disorders observed at our institution.

Abstracts

| Table 1. Patient mean age gender with corresponding SPEP result. |
|--------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
|                      | Acute inflammation | Chronic inflammation | Inconclusive | Monoclonal band | Normal | Polyclonal band |                 |
| No. patients         | 2 (2%)           | 3 (6%)            | 24 (48%)     | 16 (32%)       | 3 (6%)      | 3 (6%)         |                 |
| Age (mean)           | 37              | 48               | 49            | 69             | 69           | 58             |
| Gender (M/F)         | 0.1             | 1.2              | 1.3           | 1.4            | 0.1          | 1.2            |

MP9 SINO-NASAL 5 QUESTIONNAIRE PREDICTS POOR ASTHMA CONTROL IN CHILDREN WITH PERSISTENT ASTHMA

G Phull, D Prue, C Martinez, K Scheffey, D Pillai. Children’s National Health System, Washington, DC, United States

10.1136/jm-2016-000080.21

Purpose of Study Up to 80% of asthmatic children may experience upper airway symptoms, including rhinitis, often perceived as coming from lower airways. Asthma diagnosis, classification and assessment of control are defined by the National Asthma Education Prevention Program (NAEPP) 2007 guidelines, but may underestimate the impact of the upper airway. We explored associations between Sino-Nasal 5 (SN-5) quality of life questionnaire, validated in radiographic confirmed sinus disease, and NAEPP asthma impairment in children. We hypothesize that children with NAEPP defined uncontrolled asthma will have abnormal SN-5 scores.

Methods Used We performed a retrospective chart review of children (1–21 yr) referred to a pediatric pulmonary clinic for persistent asthma. Data collected include age, gender, BMI%, NAEPP asthma severity, SN-5, asthma control (TRACK children ≤5 y, ACT children ≥5 y) and pulmonary function testing (PFT). The primary analysis was to identify associations between SN-5 scores and levels of NAEPP guideline impairment: daytime symptoms, night time awakenings, activity interference and PFTs. Significant SN-5 scoring was defined as ≥3.5 based on prior studies. PFT was performed in children ≥5 y. Statistical analysis with SPSS 22.

Summary of Results 76 children were evaluated; 38% female, mean age 6.9 y and mean BMI% 69%. Significant SN-5 score (≥3.5 vs. <3.5) was associated with decreased control of daytime symptoms (OR 0.16 [95% CI:0.06–0.44]), night time awakenings (OR 0.09 [0.03–0.29]), activity interference (OR 0.2 [0.06–0.68]) and asthma control (OR 0.32 [0.12–0.83]). Those with SN-5 ≥3.5 had poor asthma control based on TRACK (p<0.002) and ACT (p<0.001). Age, gender, BMI%, asthma severity and PFTs were not associated with SN-5.

Conclusions In persistent asthmatic children, NAEPP defined daytime, night time, activity related impairment and poor asthma control were associated with a significant SN-5 score; PFTs and NAEPP asthma severity were not. This suggests that upper airways may play a larger role in lower airway associated symptoms, and that SN-5 may be beneficial in assessing asthma symptoms. Recognizing and treating upper airway symptoms, an understated area in asthma guidelines, might improve overall asthma control. A prospective analysis in a larger cohort is recommended to evaluate these findings.

MP10 ANALYTICAL STYLE PREDICTS RELIGIOUS AND TELEOLOGICAL BELIEF

SM Steiner, JC Zemla, S Sloman. Cognitive, Linguistic, and Psychological Sciences, Brown University, Providence, RI, United States

10.1136/jm-2016-000080.22

Purpose of Study Shenhav et al. (2011) found that individual analytical style (reflective vs. intuitive) predicts belief in God or a higher power. Although intuitive thinkers are more likely to have strengthened religious beliefs since childhood, there is no correlation between analytical style and familial religiosity during childhood. This study examines the hypothesis that the link between intuitive thinking and religious belief is part of a broader preference for teleological explanations. We also test a possible mechanism responsible for teleological endorsement: intuitive thinkers may endorse teleological explanations because they confuse causal directionality.

Methods Used A questionnaire comprised of a randomized series of stimuli was administered via Amazon Mechanical Turk. Stimuli included the Cognitive Reflection Test (CRT; Frederick, 2005) to determine analytical style, questions on conditional probability to judge causal reasoning (Kahneman & Tversky, 1977), and a series of true or false questions on various teleological statements (Kelemen et al., 2013). Participants were then asked to rank on a scale from 1–7 the extent to which they believe in the existence of God or a higher power, and the extent to which they believe such a higher power influences events in the world (agency). Statistical analysis was performed using Spearman correlation.

Summary of Results As expected, teleological endorsement levels positively predicted belief in agency of a higher
power (R=0.28, p<.01) and CRT score negatively predicted teleological endorsement levels (R=−0.24, p<.01). Individual belief in agency of a higher power predicts teleological tendencies to a greater extent than religious belief alone (R=0.075) for belief in higher power, compared with p=0.885 for belief in agency of higher power.

Conclusions Our results replicate previous findings that show a relationship between intuitive thinking and religious beliefs and suggest that this may reflect a general preference for teleological explanations. However, the reasons why intuitive thinkers endorse teleological explanations are still unclear.

**MP11**

**COMORBID DEPRESSION OR ANXIETY IS ASSOCIATED WITH AORTIC VASCULAR INFLAMMATION AND CORONARY HEART DISEASE BEYOND TRADITIONAL CARDIOVASCULAR RISK FACTORS IN PSORIASIS**

T Aberra, A Joshi, J Lerman, J Rodante, J Silverman, T Aridi, M Chen, M Playford, N Mehta. National Heart Lung and Blood Institute, National Institutes of Health, Bethesda, MD, United States

10.1136/jim-2016-000080.23

**Purpose of Study** Psoriasis is a chronic inflammatory disorder associated with vascular inflammation (VI), measured by 18-fluorodeoxyglucose positron emission tomography/computed tomography (18-FDG PET/CT), and increased risk of MI. Patients with psoriasis are more likely to have comorbid depression and anxiety. Whether these comorbidities accelerate the development of CVD in psoriasis is unclear. We hypothesized that aortic VI and coronary plaque burden would be increased in patients with psoriasis who have depression and/or anxiety compared to those with psoriasis who do not.

**Methods Used** Patients were prospectively enrolled. Those who reported a history of depression and/or anxiety (n=40) on survey and age- and gender-matched patients who reported no history of psychiatric illness (n=40) were selected. Target-to-Background ratio from 18FDG PET/CT was used to assess aortic VI, and coronary CT angiography scans were analyzed for coronary plaque composition.

**Summary of Results** Both aortic VI and coronary plaque burden were higher in psoriasis patients with comorbid depression or anxiety compared to those without (table 1). After adjustment for Framingham Risk Score, body mass index, and statin use; VI (β=0.24, p=0.02), total plaque burden (β=0.13, p=0.04), and non-calcified burden (β=0.13, p=0.04) were associated with comorbid depression and/or anxiety.

**Conclusions** Patients with psoriasis who have comorbid depression or anxiety have increased aortic VI and coronary plaque burden, suggesting that identification of psychiatric diagnoses in psoriasis may be warranted for future CV risk reduction in this high risk population.

**MP12**

**CRYOGLOBULINEMIA IN A PATIENT WITH CHRONIC LYMPHOCYTIC LEUKEMIA (CLL)–A CASE REPORT AND REVIEW OF LITERATURE OF RENAL INVOLVEMENT IN CLL**

S Arora, D Levitan, N Regmi, G Sidhu, R Gupta, A Nacastri, S Saggi, A Braverman. 1. Medicine, SUNY Downstate, Brooklyn, NY, United States; 2. Pathology, SUNY Downstate, Brooklyn, NY, United States

10.1136/jim-2016-000080.24

**Purpose of Study** We report a case of early stage CLL that caused cryoglobulinemia-related glomerulonephritis (MPGN). This prompted a literature review to identify the incidence and causes of renal disease in patients with CLL.

**Methods Used** Using a PUBMED search data of cases reported between 1990 and 2014, we selected cases with the following criteria:

1. Clinical and hematologic diagnosis of CLL
2. Evidence of renal insufficiency in association with CLL in the absence of other causes for proteinuria.

**Table 1: Characteristics of Study Groups**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Depression and/or Anxiety Diagnosed (n=40)</th>
<th>No Psychiatric Diagnoses (n=20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographic and Clinical Characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>61.1±11.0</td>
<td>49.9±13.0</td>
<td>.006</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>23 (58%)</td>
<td>16 (80%)</td>
<td>.20</td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>28.9±5.3</td>
<td>28.8±5.5</td>
<td>.91</td>
</tr>
<tr>
<td>Metabolic syndrome</td>
<td>19 (48%)</td>
<td>10 (50%)</td>
<td>.67</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>13 (33%)</td>
<td>12 (60%)</td>
<td>.12</td>
</tr>
<tr>
<td>Type 2 Diabetes, n (%)</td>
<td>4 (10%)</td>
<td>2 (10%)</td>
<td>.91</td>
</tr>
<tr>
<td>Hypercholesterolemia, n (%)</td>
<td>27 (68%)</td>
<td>20 (60%)</td>
<td>.31</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>7 (18%)</td>
<td>5 (25%)</td>
<td>.39</td>
</tr>
<tr>
<td>CBC and Hematocrit Risk Profile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Satelite cr. mm/lt</td>
<td>124±115.7</td>
<td>120±116.8</td>
<td>.92</td>
</tr>
<tr>
<td>Cholesterol, mg/dl</td>
<td>173±82.0</td>
<td>172±82.9</td>
<td>.15</td>
</tr>
<tr>
<td>Total Uric Acid, mg/dl</td>
<td>4.84±2.82</td>
<td>4.18±2.60</td>
<td>.22</td>
</tr>
<tr>
<td>Hct, %</td>
<td>86.9±9.1</td>
<td>86.8±9.1</td>
<td>.91</td>
</tr>
<tr>
<td>Fe, ug/dl</td>
<td>109±6.4</td>
<td>109±6.1</td>
<td>.95</td>
</tr>
<tr>
<td>Platelet Count, x10³</td>
<td>150±55.5</td>
<td>150±55.5</td>
<td>.95</td>
</tr>
<tr>
<td>Proteinuria Risk Score [n=20]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IFE of cryoglobulins involving the kidney in our patient; predominantly IgG and kappa light chain (A&amp;D) with weak expression of IgM lambda (B&amp;D).</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Abstract MP11 Figure 1**
Summary of Results Review of the literature revealed that 50 cases of CLL-related nephropathy have been reported, commonly with the nephrotic syndrome (MPGN). IHC staining of the renal biopsies of these patients revealed mostly monoclonal IgG kappa. Many of these were low stage CLL patients and had not been treated. In 68% the renal complications first developed years after the CLL was diagnosed. Most importantly, 65% of all patients’ nephropathies responded completely to anti-CLL therapy.

Conclusions We report a rare manifestation of a secretory type of CLL with cryoglobulinemic vasculitis; leading to rapid renal deterioration needing dialysis. Renal damage can be a sequela of early-stage CLL due to its secretory phenotype. Timely recognition of kidney impairment and routine testing of serum or urine proteins in CLL patients is warranted to detect its early transition to a secretory phenotype. We believe that therapeutic intervention in early stage CLL may be effective in the preservation of renal function by removing the secretory phenotypic clone.

MP13 IMPORTANT ROLE OF PROTHROMBIN TIME (PT) AND PARTIAL THROMBOPLASTIN TIME (PTT) IN PREDICTING TPA-RELATED HEMORRHAGIC TRANSFORMATION

W Deng, T Wickham, D McMullin, K Feeney, FS Buonanno, EH Lo, M Ning. Neurology, Massachusetts General Hospital, Boston, MA, United States
10.1136/jim-2016-000080.25

Purpose of Study IV tPA is not routinely followed by blood work due to its reputed short half life. While there has been much focus on tPA’s extra-vascular effects on the neurovascular unit in the context of hemorrhagic transformation (HT), little is known about its intravascular efficacy, where it has its intended effect. Emerging data suggest that tPA may be most effective in microvasculature and IV therapy may be a good adjunct to intra-arterial therapy. We previously found that the effect of tPA can last more than 72 hr after stroke onset. Now, we report that even routine blood labs can potentially predict HT.

Methods Used 72 stroke patients with IV tPA were recruited on IRB approval. Clinical coagulation profile (PT, PTT, fibrinogen and D-dimer) were performed at 12, 24, 72 hr post tPA. Patients on medications (e.g. anticoagulants) or with conditions (e.g. liver dysfunction, infection) that may affect these labs were excluded.

Summary of Results Compared to those without HT, HT patients had significantly higher PT and PTT (Fig A,B) as early as 12 hr post IV tPA and throughout the first 3 days of treatment. ROC analysis suggested PT/PTT at 12 and 24 hr has potential to predict tPA-induced HT (Fig C,D. PT: AUC=0.848, p=0.001; PTT: AUC=0.877; p=0.003).

Conclusions Higher PT/PTT level within 72 hr of IV tPA is early marker of tPA-induced HT. Whether these routine labs have value in symptomatic hemorrhage will require further study in a larger cohort. But this proof-of-concept study suggests that tPA efficacy can potentially be followed in real time. The development of a reliable blood test would be of clinical utility to gauge thrombolytic efficacy in real time to guide and triage adjunct treatments.

MP14 UTILIZATION OF THE INVASIVE CARDIAC LABORATORY FOR IMMEDIATE CARDIAC CATHETERIZATION: A QUALITY IMPROVEMENT PROJECT

D Friedman, A Bierzynski, N Coplan. Lenox Hill Hospital, Jersey City, NJ, United States
10.1136/jim-2016-000080.26

Purpose of Study Immediate cardiac catheterization is indicated for patients presenting with ST elevation (STE) myocardial infarction, and door-to-balloon time should be <90 min. Patients with non-ST elevation myocardial infarction (NSTEMI) can often be stabilized with medication, and only require urgent invasive evaluation if there is persistent chest pain(despite medical therapy) or hemodynamic or electrical instability. Immediate cardiac catheterization for patients presenting to the ER with chest pain is available in many hospitals, but it involves a large investment of resources which need to be properly utilized. This study evaluated patients sent for urgent invasive evaluation to determine how the facility is utilized.

Methods Used In a retrospective chart review, charts from all STEMI code patients presenting between the dates 1/1/15–9/1/15 were studied. The presenting EKG was evaluated to determine whether STE criteria (as per ACC guidelines) were met. The charts were reviewed for angiographic

Abstract MP13 Table 1

<table>
<thead>
<tr>
<th></th>
<th>ST+</th>
<th>ST-</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥90%</td>
<td>29</td>
<td>10</td>
</tr>
<tr>
<td>&lt;90%</td>
<td>4</td>
<td>7</td>
</tr>
</tbody>
</table>
data to determine whether there was ≥90% stenosis of a coronary artery (≥90%) or not (≤90%). Clinical parameters were studied to determine if there were any differences between the groups.

Summary of Results The study group included 50 patients who went to the cardiology catheterization lab emergently secondary to an indication of STE; 33/50 (66%) patients met guideline criteria for ST elevation (STE+) while 17/50 (34%) did not (STE−). In the STE+ group, 29/33 (88%) had ≥90% occlusion of a coronary artery, while 10/17 (59%) in the STE-group had this degree of stenosis. The sensitivity and specificity of STE for ≥90% coronary artery occlusion on angiography was 74% and 64% respectively. The PPV of STE for >90% stenosis was 88%, while the NPV was 41%.

Conclusions Significant STE in the proper clinical situation is a Class 1 indication for immediate coronary catheterization. However, 34% referred for immediate coronary catheterization in this study did not meet ACC criteria for STEMI. Although a significant % in the NSTEMI group had ≥90% stenosis, urgent catheterization is only indicated in this group when there is a clinical parameter which dictates the necessity of immediate evaluation.

MP15  PEDIATRIC SLEEP QUESTIONNAIRE DETECTS SLEEP DISORDERED BREATHING IN ASTHMATICS WITH POOR NIGHTTIME CONTROL

R Megalaa, G Phull, D Prue, K Scheffey, D Pillai. Children’s National Health System, Washington, DC, United States 10.1136/jim-2016-000080.27

Purpose of Study Up to 35% of asthmatic children have degrees of sleep disordered breathing (SDB) which may be perceived as uncontrolled asthma. Asthma diagnosis, classification and assessment of control are defined by the National Asthma Education Prevention Program (NAEPP) 2007 guidelines and include nighttime awakenings as one asthma impairment category. Unclear whether this stems from asthma or SDB. The Pediatric Sleep Questionnaire (PSQ) is validated to identify SDB in children; however associations with specific levels of NAEPP guideline’s asthma related impairment have not been evaluated. We hypothesize that asthmatic children with impairment only in NAEPP nighttime awakenings, but not other categories, will have a positive PSQ score (>0.33), suggesting screening for SDB.

Methods Used We performed a retrospective chart review of children (age 1–21 yrs) referred to a pediatric pulmonary clinic. Data collected included age, gender, BMI%, spirometry, PSQ, asthma control (TRACK <5 yrs, ACT ≥5 yrs), and NAEPP asthma severity, control and impairment. Significant PSQ scoring is >0.33 based on previous validation. Spirometry was performed in children ≥5 yrs. Statistical analysis performed with SPSS 22.

Summary of Results 76 inner-city children were included in this study; 38% female, mean age 6.9 yrs; and mean BMI % 69%. Significant PSQ scoring (>0.33 vs ≤0.33) was associated with night time awakenings (OR 11.4 [95% CI:3.7–35.2]) and decreased asthma control seen in TRACK (p<0.003) and ACT questionnaires (p<0.001). Overweight/obese status (BMI% ≥85), spirometry, asthma severity, activity interference and daytime symptoms were not associated with a significant PSQ score.

Conclusions In asthmatic children, impairment in night time awakenings as defined by NAEPP guidelines was associated with a significant PSQ score, and poor asthma control, based on abnormal TRACK and ACT scores, however other NAEPP categories of impairment; daytime symptoms, activity interference, asthma severity and control, were not. This suggests that screening SDB with the PSQ in children with night time awakenings based on NAEPP criteria may detect underlying SDB. This may lead to further investigations, treatment and subsequent improvement in asthma symptoms. A prospective analysis in a larger cohort is recommended to validate these findings.

MP16  SCREENING FOR INFECTIVE ENDOCARDITIS AMONG PATIENTS IN AN INNER CITY HOSPITAL

R Sharma, E Gang, D Conaway, M Gang. 1 Kansas City University of Medicine and Biosciences, Kansas City, MO, United States; 2 Nebraska Heart Institute, Hastings, NE, United States; 3 University of Missouri Kansas City, Kansas City, MO, United States 10.1136/jim-2016-000080.28

Purpose of Study Over the years, epidemiology of infective endocarditis (IE) has been changing with the change in population at risk. The aging of our population, better antibiotics for treatment of infections and changes in predisposing conditions have contributed to the changing prevalence patterns of this disease in different patient groups. At present little data is available on the prevalence of IE in selected patient groups such as the medically indigent. We studied the prevalence of IE in patients evaluated in an inner city hospital.

Methods Used We screened the clinical, laboratory and echocardiographic data of 246 consecutive patients referred for echocardiographic evaluation, with suspected IE during the period 04/1996 to 05/2001. Using the New Duke criteria for diagnosing endocarditis, these patients were classified as having 1. Definite IE 2. Possible IE and 3. Diagnosis of IE rejected.

Summary of Results Of the 246 patients screened, 72 (29%) fulfilled criteria for diagnosis of IE. Twenty of these patients (8%) were classified as “definite” IE and 52 (21%) as “possible” IE. Diagnosis of IE was “rejected” in 174 (71%) of the screened patients.

Conclusions Screening for IE in this medically indigent patient population of an inner city hospital, confirmed definite endocarditis in only 8% of the patients referred with suspected endocarditis. This represents a very small proportion of the patients screened and is much lower than reported in other studies, in a different patient population. This could be due to a higher degree of suspicion for IE in this patient group. Further inquiry is needed to confirm the underlying mechanism responsible for this observation.

J Investig Med 2016;64:800–825 811
Abstracts

AFMR Presidential Plenary Session
(Scientific Session II)
1:05 PM – 3:05 PM
Wednesday, April 13, 2016

13 LOW BODY MASS INDEX DIABETES IS CHARACTERIZED BY IMPAIRED INSULIN SECRETION

A Tiwari,1 RD Gupta,2 M Carey,1 A Wickramanayake,1 CM Kocherlakota,2 N Thomas,2 M Hawkins1. 1Endocrinology, Albert Einstein College of Medicine, Bronx, NY, United States; 2Endocrinology, Christian Medical College, Vellore, India

Purpose of Study Fibrocalculous Pancreatic Diabetes (FCPD) and Lean Diabetes (LD) are unique forms of diabetes affecting millions of people in developing countries, characterized by the presence or absence of pancreatic calcifications on ultrasound and insulin-requiring but ketosis-resistant diabetes. To optimize therapeutic strategies for FCPD and lean diabetes patients, it is imperative to conclusively assess their insulin secretion using gold-standard methodologies.

Methods Used Comprehensive tests were undertaken in n=22 Indian males with FCPD (age 30±2 y, BMI 19.7±0.6 kg/m2, HbA1c 9.0±0.3%) and n=6 with LD (age 36±4 y, BMI 18.3±0.1 kg/m2, HbA1c 11.6±1.3%), and compared with n=12 age, BMI matched ND, n=16 T1D (HbA1c 9.1±0.3%) and n=12 T2D subjects (age 36±2 y, BMI 26.0±0.3 kg/m2, HbA1c 9.7±0.6%). Following correction of hyperglycemia for over two weeks, mixed-meal tolerance tests (MMTT) and C-peptide deconvolution analysis was performed to assess beta-cell function.

Summary of Results Glucose and C-peptide responses to MMTT suggest subjects with FCPD (14.5±2.2 pmol/kg/min) and LD (15.0±2.9 pmol/kg/min) have markedly impaired insulin secretion relative to both ND and T2D (p<0.001), and not statistically different from T1D (figure 1).

Conclusions Thus, we report the first studies showing that patients with low BMI diabetes have impaired insulin secretion despite correction of hyperglycemia, consistent with nutritional effects on beta cell development or function.

15 PFO CLOSURE REDUCES PLASMA LEVELS OF SEROTONIN IN A LONG TERM FOLLOWUP OF STROKE PATIENTS

W Deng, D McMullin, T Wickham, K Feeney, I Inglessis, I Palacios, FS Buonanno, EH Lo, M Ning. Neurology, Massachusetts General Hospital, Boston, MA, United States

Purpose of Study PFO allows venous clots and vasoactive factors to bypass pulmonary filtration and remain in circulation. We previously identified an immediate reduction of procoagulant serotonin (5-HT) in left atrial blood post PFO closure. To understand the long-term effect of PFO closure, we report the change of 5-HT in peripheral venous blood in 1-year followup.

Methods Used 97 PFO-related stroke patients were recruited on IRB approval. Venous blood was collected at baseline (BL) and 1 year follow-up (FU) of treatments (PFO closure and medical therapy). Plasma 5-HT was quantified by mass spectrometry. Patients with serotonin modifying medications (ie, SSRIs) or conditions (anxiety/depression) were excluded.

Summary of Results 5-HT level in peripheral venous blood was significantly reduced by 27.27% (BL: 7.57 pmol/L; FU: 5.46 pmol/L, p=0.0034) after PFO closure.

Abstracts 13 Figure 1

Abstract 15 Figure 1
POSTPARTUM DEPRESSION SCREENING IN A PEDIATRIC ED
L Jarvis, G Badolato, K Breslin, M Goyal. Emergency Medicine, Children’s National Health System, Washington, DC, United States
10.1136/jim-2016-000080.32

Purpose of Study Postpartum depression (PPD) occurs in up to 20% of mothers. The American Academy of Pediatrics recommends routine screening for PPD. The pediatric emergency department (PED) serves as a safety-net for vulnerable, high-risk populations, and may be a useful site for screening. This study investigates (1) prevalence of PPD positive screens, (2) factors associated with a positive PPD screen, (3) frequency of mothers who had not completed a PPD screen previously, and (3) acceptability and impact of PPD screening.

Methods Used We performed a prospective, cross-sectional survey of a convenience sample of mothers of infants <6 months of age presenting with low-acuity complaints. Mothers completed a computerized survey that included a validated PPD screening tool (Edinburgh Postnatal Depression Scale). We calculated frequency of positive screens and performed bivariable logistic regression to identify factors associated with a positive PPD screen. PPD positive-screened mothers were contacted for phone follow-up at one-month.

Summary of Results 121 mothers were screened for PPD (mean age=28±6 years; 86% English vs. Spanish language; 50% non-Hispanic Black race/ethnicity; 75% non-private insurance) during presentation to the ED with their infant (mean age=3±2 months; 51% female). Twenty-seven mothers (22%) screened positive for PPD with eight mothers (7%) reporting suicidal thoughts. Forty-seven percent (57/121) of mothers had never previously been screened, including 59% (16/27) of PPD-positive screened and those endorsing suicidal thoughts (5/8, 63%). Infants of PPD-screened positive mothers had more ED visits than those whose mothers screened negative (median 2 vs. 1). Seventy-four percent (90/121) of participants viewed ED-based PPD screening favorably. At one-month follow-up 100% (n=12) reported ED-based PPD screening acceptable and the majority endorsed positive impact of screening, including increased access to support (8/12, 67%) and improved activities of daily living (10/12, 83%).

Conclusions PPD is reported by approximately 1 in 5 mothers in an urban PED and the majority of PED-screen positive mothers had not been screened previously. PED-based screening was well-accepted and had a positive impact. Our study informs future efforts for interventions to support mothers of young infants who use the PED for care.
Abstracts

18 IMPROVEMENT IN PSORIASIS SKIN DISEASE SEVERITY IS ASSOCIATED WITH REDUCTION OF CORONARY PLAQUE BURDEN
J B Lerman, a AA Joshi, J Rodante, T Albera, MT Kabbany, TF Sahlahuddin, Q Ng, J Silverman, MT Chen, NN Mehta. National Heart, Lung and Blood Institute (NHLBI), Washington, DC, United States

Purpose of Study Psoriasis (PSO), a chronic inflammatory disease associated with increased cardiovascular (CV) risk, provides a clinical human model to study inflammatory atherogenesis. While PSO severity is associated with both in vivo vascular disease and future CV risk, the longitudinal impact of PSO severity on coronary disease progression is unknown. We hypothesized that an improvement in PSO severity may lead to a reduction in coronary plaque burden by coronary CT angiography (CCTA).

Methods Used Consecutively recruited PSO patients (N=50) underwent CCTA (320 detector row, Toshiba) and cardiometabolic profiling at baseline and 1-year follow-up. Total (TB) and non-calcified (NCB) coronary plaque burden were quantified using QAngio (Medis, Netherlands). PSO severity was measured as the psoriasis severity index (PASI). The longitudinal change in coronary plaque burden was analyzed with unadjusted and adjusted regression.

Summary of Results The cohort had a low Framingham Risk Score and mild to moderate PSO. Patients whose PSO severity improved (ΔPASI =27%; p<0.001) (N=33) had significant improvement in TB (β=0.40, p=0.003) and NCB (β=0.49, p<0.001) (table 1), beyond adjustment for traditional CV risk factors, BMI, statin use, & systemic/biologic PSO therapy.

Conclusions Improvement in PSO severity was associated with improvement in coronary plaque burden by CCTA. Our study suggests that a reduction in skin inflammation may reduce the progression of early, non-calcified coronary plaque. Larger studies are needed to confirm these findings.

Table 1: Demographic and Clinical Characteristics of the Study Group, stratified by Improvement in Psoriasis Area Severity Index (PASI) Score

<table>
<thead>
<tr>
<th>Parameter</th>
<th>No Improvement in PASI or N=17</th>
<th>Improvement in PASI or N=33</th>
<th>ΔPASI</th>
<th>ΔNCB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>52.2±6.5</td>
<td>53.3±14.4</td>
<td>-0.04</td>
<td>-0.89</td>
</tr>
<tr>
<td>Male, %</td>
<td>51.8%</td>
<td>-</td>
<td>61.8%</td>
<td>10.0%</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>6.0%</td>
<td>3.0%</td>
<td>-0.00</td>
<td>11.8%</td>
</tr>
<tr>
<td>Heart Disease, %</td>
<td>8.0%</td>
<td>1.0%</td>
<td>-0.00</td>
<td>1.0%</td>
</tr>
<tr>
<td>Hypocalcemia, %</td>
<td>12.0%</td>
<td>0.0%</td>
<td>-0.00</td>
<td>1.0%</td>
</tr>
<tr>
<td>Current Smoker, %</td>
<td>2.0%</td>
<td>3.0%</td>
<td>0.05</td>
<td>3.0%</td>
</tr>
<tr>
<td>Risk Factor Index</td>
<td>20.0±7.0</td>
<td>20.0±9.0</td>
<td>0.00</td>
<td>20.0±9.0</td>
</tr>
</tbody>
</table>

Resveratrol improves insulin resistance with anti-inflammatory and “browning” effects in adipose tissue of overweight humans
R Gospin, O Sandu, K Gambina, ATiwar, MBonkowski, M Hawkins
1Endocrinology, Albert Einstein College of Medicine, Bronx, NY, United States; 2Harvard Medical School, Boston, MA, United States

Purpose of Study Resveratrol is a plant-derived polyphenol whose beneficial metabolic effects in rodents include improved insulin sensitivity, reduced inflammation, and increased muscle mitochondrial biogenesis. We set out to confirm these findings in insulin resistant human subjects, by examining the effects of resveratrol on insulin sensitivity, muscle mitochondria, and adipose inflammation.

Methods Used Specifically, resveratrol 2 gm/day (RV) or placebo (PL) were administered for 28 days in a randomized, double-blinded fashion to n=21 non-diabetic subjects (17 M; Age=52±2; BMI=31.9±0.9 kg/m²; HOMA-IR=3.9±0.2). All subjects participated in 6-hour, stepped euglycemic hyperinsulinemic (30 and 80 mU/m² min) ‘pancreatic clamp’ studies to assess hepatic and peripheral insulin sensitivity; with biopsies of vastus lateralis muscle and subcutaneous abdominal adipose tissue, before and after RV and PL. Muscle mitochondria were analyzed for quantity, size, area in a field, and the % area covered, using electron microscopy with Velocity image analysis.

Summary of Results RV induced a 22% (p=0.035) increase in glucose uptake, but did not affect glucose production. There were no changes in quantity (p=0.829) or percent area (p=0.897) of muscle mitochondria. There were no changes in basal or resting energy expenditure (Kcal/day) or respiratory quotient, as assessed by indirect calorimetry (Deltatrac), or in muscle strength in these healthy middle-aged subjects. However, RV reduced adipose tissue inflammation, with decreased expression of the pro-inflammatory cytokines TNFα and IL6 in whole fat (by 68% and 52%, p<0.05), and of IL6 and PAI-1 in adipose macrophages (by 50% and 40%, p<0.05). Adiponectin expression in whole fat increased by 53% with RV. Furthermore, we observed increased expression of genes associated with “browning” of adipose tissue, including UCP1 and PGC-1α (46.6% and 34.9% increases, respectively).

Abstract 18 Figure 1 *P-value is calculated by comparing baseline and 1-year follow-up values for variables using paired t-test for continuous variables, and Pearson’s chi-squared test for categorical variables. All values are expressed as Means±SD, unless specified otherwise. PASI: Psoriasis Area Severity Index.

Abstract 19 Improvement in PSO severity was associated with improvement in coronary plaque burden by CCTA. Our study suggests that a reduction in skin inflammation may reduce the progression of early, non-calcified coronary plaque. Larger studies are needed to confirm these findings.
Conclusions Thus, while improved insulin sensitivity was not accompanied by changes in size or number of muscle mitochondria, anti-inflammatory and ‘browning’ effects in adipose tissue could contribute to resveratrol’s favorable metabolic effects in insulin resistant humans.

20 NASOPHARYNX MICROBIOME COMPOSITION VARIES OVER TIME IN PEDIATRIC ASTHMA
M Perez-Losada,1,2 A Goldstein,1 L Alamri,1 KA Crandall,7 R J Freishtat.1 1Children’s Research Institute, Children’s National Medical Center, Washington, DC, United States; 2CBI, GWU, Ashburn, VA, United States
10.1136/jim-2016-00080.36

Purpose of Study The application of next-generation sequencing (NGS) technology has shown that microbial communities in the respiratory airways (i.e., the microbiome) play a significant role in the onset, development and severity of asthma. However, little is known about their temporal dynamics (i.e., microbial succession), which poses a significant obstacle to identifying pulmotypes of disease and assessing inter-patient variation. Here, we couple NGS and 16S rRNA data to characterize the nasopharynx microbiome of children with asthma and determine its stability over time.

Methods Used We collected nasal washes from 40 children with asthma enrolled in the AsthMaP-2 Project from two consecutive visits, six months apart. Total DNA was extracted and sequenced for the 16S-V4 rRNA gene region (~250 bp) using the MySeq Illumina platform. Reads were analyzed in Mothur using the SILVAV119 reference database. Alpha diversity metrics and phylogenetic and count-based distance community indexes of beta diversity were compared across samples and time points. PCoA and NJ clustering analysis were used to assess community relatedness. Differences in alpha diversity and OTU abundance between sample pairs across time points were also compared.

Summary of Results A mean of 27,479 clean 16S sequences were generated per sample, respectively. Genera such as Moraxella, Corynebacterium, Prevotella, Staphylococcus, Alloprevotella, Streptococcus, Peptoniphilus, Fusobacterium, and Haemophilus accounted for 36 to 99% of the reads across samples. These genera have been previously found in the nasopharynx of asthmatic and healthy children. A total of 61 OTUs from these genera were present in at least 50% of the samples (i.e., the nasal core microbiome). Significant differences in core microbiome composition were detected between sample pairs, but no directional trend (increase or decrease) was observed across sample pairs. Samples were randomly ordinated and did not cluster together.

Conclusions Our analysis of nasal microbiomes in 40 asthmatic children revealed significant differences in composition within individuals over six months. Future cross-sectional microbiome studies need to be aware of short span temporal dynamics in nasal microbiota.

21 DETERMINANTS OF VASCULAR INFLAMMATION BY 18-FLUORODEOXYGLUCOSE PET/MRI: FINDINGS FROM THE PSORIASIS, ATHEROSCLEROSIS AND CARDIOMETABOLIC DISEASE INITIATIVE
MT Kabbany,* AA Joshu, M Ahihman, J Rodante, JB Lerman, T Abena, J Silverman, A Dahiya, DA Bluemke, MP Playford, NN Mehta. National Heart, Lung and Blood Institute, Bethesda, MD, United States
10.1136/jim-2016-00080.37

Purpose of Study Psoriasis (PSO), a chronic inflammatory disease associated with increased CV risk, provides a clinical human model to study inflammatory atherogenesis. We aimed to assess the major determinants of vascular inflammation (VI) measured by 18FDG PET-MRI in a well-phenotyped PSO cohort.

Methods Used 124 consecutive patients with PSO underwent 18FDG PET-MRI scans. We used target-to-background ratio to quantify VI 120 minutes post FDG injection. Homeostatic model assessment of insulin resistance (HOMA-IR) was measured, along with cholesterol efflux capacity (CEC) and HDL particle concentration by NMR (Liposcience) fasting.

Summary of Results Our cohort was middle aged (mean 49±13.3 years) with mild to moderate PSO, and low CV risk (median Framingham Risk Score (FRS) 2, IQR 2–6). PSO was associated with increased VI (β=0.27, p<0.005), compared to healthy controls. VI was associated with HOMA-IR (β=0.26, p<0.001), CEC (β=−0.12, p=0.04) and HDL particle concentration (β=−0.19, p=0.003) beyond traditional CV risk factors (age, gender, FRS and BMI). Among these, HOMA-IR provided maximum incremental value in predicting VI beyond traditional risk factors (χ2=39.36, p<0.001).

Conclusions VI by FDG PET MRI is associated with traditional CV risk factors and cardiometabolic parameters.
Insulin resistance and CEC were most strongly associated with VI by FDG PET-MRI beyond traditional CV risk factors and BMI in PSO suggesting that cardiometabolic disease increases CV risk in PSO.

**Conclusion**

Cumulative analysis shows mitotic synchrony. Additionally, blocking TGF-β1 secretion and a pro-inflammatory/pro-fibrotic airway. This finding establishes rationale for targeting progenitor cell mitotic behavior rather than immune-mediated inflammation in fibrotic disease.

**Purpose of Study**

Mitotic behaviors are likely important for maintaining and restoring homeostasis in lung diseases with epithelial injury. We recently proposed that regenerative asynchrony in repairing 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 and then resynchronized via capture of the G1/S checkpoint via pulse exposure to dexamethasone, simvastatin, or aphidicolin. Experiments utilized a novel method we developed for inducing mitotic asynchrony in normal progenitors. Induced populations were used to elucidate if TGF-β1 plays a role in the resynchronization process.

**Summary of Results**

Human asthmatic fully-differentiated air–liquid interface airway epithelial mitosis was asynchronous relative to normal epithelia. Mitotic capture increased the percentage of progenitors in G1. This resynchronization in the asthmatic epithelium reduced basolateral TGF-β1 secretion. We next examined whether inducing mitotic asynchrony in normal epithelial cells would result in TGF-β1 secretion. Mitotic asynchrony was induced and samples showed moderate asynchrony at 6 and 12 hours that resolved spontaneously by 48 hours. These cells show 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 through contact and non-contact dependent experiments. Additionally, blocking TGF-β1 delays resynchronization.

**Conclusions**

Cumulative analysis shows mitotic synchrony is the homeostatic state in airway epithelial progenitor populations and poorly-synchronized mitosis (as in asthma) induces TGF-β1 secretion and a pro-inflammatory/pro-fibrotic airway. This finding establishes rationale for targeting progenitor cell mitotic behavior rather than immune-mediated inflammation in fibrotic disease.

**Purpose of Study**

Psoriasis (PSO), a chronic inflammatory skin disease, is associated with increased CV risk and vascular inflammation (VI). However, the effect of therapeutic lifestyle changes (TLC) including exercise on VI over time is unknown. We hypothesized that TLC would lead to an improvement in VI at 1 year accompanied by improvements in aortic wall characteristics.

**Methods Used**

65 PSO patients, recruited consecutively, underwent FDG PET/CT, phase contrast MRI scans and clinical visits for evaluation of VI, wall characteristics and exercise frequency, at baseline and 1 year follow-up. VI was measured as Target-to-background ratio (TBR), and aortic distensibility (AD) and wall thickness were assessed by commercial software on phase contrast MRI scans. Clinical parameters were ascertained by both survey and provider.

**Summary of Results**

VI decreased at 1 year (6.5% decrease in TBR; p<0.0001), and was inversely associated with exercise frequency beyond adjustment for CV risk factors (β=−0.27; p=0.001). Furthermore, this decrease in VI was associated with improvement in AD (40% increase; p<0.001) and aortic wall thickness (8.5% decrease; p<0.001).

**Conclusions**

Our findings suggest that VI improves with TLC. This 6.5% decrease in VI could lead to ~30% reduction in future adverse events, based on a recent large prospective study. This VI reduction is also associated with improved aortic wall characteristics suggesting that targeting VI as a surrogate marker holds promise to understand the effects of TLC on CV disease.

**Abstract 23 Figure 1**
Purpose of Study Cocaine-related chest discomfort is frequently encountered in urban emergency departments. Incidence of co-morbid illness and heart disease is not well defined in patients with cocaine-related ACS. Appropriate risk stratification in patients with cocaine-related ACS is not clearly defined.

Methods Used 231 consecutive patients meeting inclusion criteria were entered into a large ACS registry at an urban, inner-city acute-care facility. Comparisons in demographics, co-morbid conditions, left ventricular function and coronary disease were made between patients with cocaine-related ACS and those with non-cocaine ACS.

Summary of Results 44 (19%) of these patients either tested positive for cocaine by urine drug screen or had self-reported cocaine abuse. Compared to the non-cocaine ACS patients, these individuals were significantly younger, more likely to be male, unmarried, uninsured and also have history of alcohol and tobacco abuse (all p<0.05). The cocaine users were less likely to have risk factors of diabetes (p<0.002) and hyperlipidemia (p<0.02). Ejection fraction mean was 51.3% (sd 15.4) in the cocaine-users vs. 48.1% (sd 14.0) in the non-cocaine users, with an incidence of EF < 40% of 28% vs. 31% respectively (p=ns), 50% (22/44) of the cocaine-users underwent a stress test evaluation, and 27% of these were positive for ischemia. Of the 41% (18/44) undergoing cardiac catheterization, 13/18 were diagnosed with significant CAD, 4/18 with non-ischemic cardiomyopathy, and one study was normal. A total of 24/44 (55%) had either a new or old diagnosis of documented CAD or NICM, compared to 94% of the non-cocaine ACS patients.

Conclusions Cocaine-related chest pain leading to hospitalization is often associated with infarction or significant coronary artery disease. Although optimal evidence-based management is lacking in this population, ischemia evaluation and appropriate further risk stratification and modification may be warranted.

Display Posters Wednesday, April 13, 2016

P1 CHOLINERGIC RECEPTOR FUNCTION IN CARDIAC ISCHEMIC PRECONDITIONING

CW Mullan,1 SA Mavropolous,1,2 K Ojamaa1,2,1 Hofstra North Shore-LIJ School of Medicine, Raleigh, NY, United States; 2The Feinstein Institute for Medical Research, Manhasset, NY, United States

Purpose of Study Cardiac acetylcholine (ACh) signaling is protective, but the role of ACh in ischemic preconditioning (IPC) remains largely unknown. We studied the effect of selective alpha-7 nicotinic ACh receptor (a7nAChR) antagonism by methylylcacantinoline (MLA) on the functional benefits of IPC and the effects of this on mitochondrial complexity and inner mitochondrial membrane potential (ψM).

Methods Used Male Sprague Dawley rats (n=17, 322±17 g) were heparinized and anesthetized with 80 mg/kg pentobarbital IP and their hearts excised and perfused at constant pressure with a non-circulating Langendorff apparatus. Left ventricular (LV) pressure (LVDP) and heart rate (HR) were continually measured with a fluid filled latex balloon attached to a pressure transducer. Treatment groups were: ischemia-reperfusion (IR)(n=6): 20 min. perfusion, 30 min. of global ischemia, 45 min. of reperfusion; IPC (n=5): 10 min. perfusion, 3 min. ischemia with 2 min. reperfusion repeated 3 times prior to IR protocol, IPC+MLA (n=6): 6 min. perfusion, 4 min. of infusion of MLA at 233 nM, IPC with MLA during reperfusion periods, then IR. Mitochondria were isolated from the LV free wall, stained for ψM and for size, and examined by Flow Cytometry with a BD LSRFortessa. Controls (C) (n=4) were freshly excised hearts from similar animals with identical anesthesia.

Summary of Results IPC increased LV work product (LVDP times HR) as a percent of pre-ischemia (%P) during reperfusion compared to IR control, and this effect was attenuated by MLA pretreatment (IR=24.1±4.5%P, IPC=49.8±2.8%P, IPC+MLA=33.8±3.5%P, p<0.01). IPC reduced end diastolic pressure from IR levels, and this was partially prevented by MLA treatment (IR=78.8±7.7 mm Hg, IPC=18.8±6.6 mm Hg, IPC+MLA=46.3±8.6 mm Hg, p<0.05). IPC maintained mitochondrial structural complexity compared to IR (C=65±6% of total mitochondria, IPC=61±5%, IR=32±4%, p<0.01). MLA reduced the effect of IPC on ψM in intact mitochondria to IR levels (IR=67±10% of intact population, IPC=88±3%, IPC+MLA=71±4%, p<0.01).

Conclusions Signaling through the a7nAChR is necessary for the effect of IPC on maintaining ψM and cardiac contractile function after IR injury.

P2 SNP ANALYSIS IN BRCA POSITIVE AND BRCA NEGATIVE SUBJECTS WITH AND WITHOUT BREAST CANCER (BRCA) REVEAL CENTRAL ROLE OF ALK SNPS AND TGFBETA SUPERFAMILY IN MALIGNANT TRANSFORMATION

I Shapira,1 R Huffman,2 E Neculiseanu,1 A Banavali,1 K Guddati,1 A Shih,2 C Mason,2 A Lee1,1 Medicine, SUNY Downstate Medical Center, Brooklyn, NY, United States; 2The Feinstein Institute for Medical Research, Manhasset, NY, United States

Purpose of Study Over 240,000 individuals are diagnosed with breast cancer each year in the USA. Outcomes depend on DNA deregulations in tumors. Carriers of deleterious BRCA1 and BRCA2 mutations are predisposed to 30 fold higher lifetime risks of breast and ovarian cancer.

Aims:
1. To check for differences in SNPs of genomic DNA obtained in BRCA +/− with and without BrCa.
2. Analyze correlates of molecular mechanisms occurring in BRCA mutant patients.
Abstracts

Methods Used We analyzed 94 subjects (41 BRCA positive) with or without BrCa to detect SNPs whose expression is significantly differentially expressed between breast cancer and controls. DNA samples were extracted from PBMCs. Samples were measured for DNA concentration using an Invitrogen QuBit Fluorometer, and diluted to 50 ng/µL.

All samples were collected between 2010 and 2014 and survival data was known in all cancer patients. Processed samples were sequenced using an Illumina MiSeq Sequencer with a 300 cycle kit to detect SNPs. Variant Call Files were analyzed in Microsoft Excel using Fisher’s Exact Test.

Summary of Results ALK SNPs were commonly found in cancer relative to control. Significant associations of ALK SNPs were seen in BRCA mutation subjects. ALK protein was overexpressed in 47% of BRCA mutations cases, which was significantly higher than in non-BRCA cases. Our results show that the ALK signaling pathway possibly is more common in early onset of breast cancer as seen with BRCA mutations. Coremine analysis showed SNPs identified in cancer were most commonly associated with deregulation of Transforming Growth Factor-Beta Superfamily protein synthesis and binding function.

Conclusions Differences in the associations of the modifying polymorphisms with BrCarisk for BRCA1 and BRCA2 mutation carriers are likely to reflect differences in the biology of tumor development in these two groups of women at high risk of breast cancer. The identification of modifying polymorphisms could therefore lead to a better understanding of the etiology of tumors in mutation carriers and also to the development of effective and more specific therapies for BrCa in mutation carriers.

P3 BURDEN OF PEDIATRIC BASAL CELL CARCINOMA NEVUS SYNDROME ON THE PATIENTS AND FAMILIES FROM THE PERSPECTIVES OF PARENTS AND GUARDIANS

FT Siddiqui, JA Solomon. University of Central Florida College of Medicine, Orlando, FL, United States; 2Ameriderm Research, Ormond Beach, FL, United States

Purpose of Study Little is known about the disease burden for children and families of children with Basal Cell Carcinoma Nevus Syndrome. Our study focused on bringing this burden to light.

Methods Used Using an internet accessible survey, we asked parents and guardians about the ways in which BCCNS has affected their families. The survey was promoted through the Basal Cell Carcinoma Syndrome Life Support Network to its membership, as well as through social media. Forty-seven parent/guardians responded.

Summary of Results It was found that at least 75% of children were diagnosed with BCCNS by the age of ten or earlier, which suggests that the burden of disease starts much earlier than previously reported. Moreover, at least 19% of parents or guardians reported that their children had 50 or more BCCs by the age of diagnosis.

Sixty-percent of patients must see five or more healthcare specialists within one calendar year, and 33% of children must go see a healthcare provider (of any specialty) 8–10 times within one calendar year.

Conclusions It is our hope that these results will help clinicians be aware of the possible diagnosis of BCCNS at earlier ages in these children. An earlier diagnosis could provide the social and medical specialty-specific support services that may prevent the development of psychosocial and other medical consequences that arise from the burden of disease of BCCNS.

P4 CIRCULATING MIRNA PROFILES POINT TO DYSREGULATION IN TGFβ/SMAD3 TUMOR SUPPRESSOR SIGNATURE IN BRCA POSITIVE BREAST CANCER PATIENTS

I Shapira, T Bhuiya, S Arora, N Mukhi, S Datla, E Neculiseanu, C Mason, A Shih, A Lee. Medicine, SUNY Downstate Medical Center, Brooklyn, NY, United States; 1The Feinstein Institute for Medical Research, Manhasset, NY, United States

Purpose of Study Over 240,000 individuals are diagnosed with breast cancer (BrCa) of which 12,000 individuals carry BRCA germline mutations. MicroRNA dysregulation is common in malignancy and may correlate with germline mutations.

Aims:
1. Analyze microRNAs in patients with breast cancer with or without BRCA germ line mutations, with and without cancer.
2. Identify molecular BRCA mutant patients to deduct reasons for accelerated malignancy.

Methods Used We analyzed plasma miR expression from 94 br cancer patients (41 BRCA positive) relative to 24 normal controls. All samples were collected between 2010 and 2014 and survival data was known for all cancer patients. TaqMan Open Array panel was used to simultaneously run hundreds of microRNA assays in the Applied Biosystem Open array real time PCR. Using AB open array real time PCR, 756 miRNA species were detected. 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 BRCA+ underepressed hasa-mir-10a and hasa-mir-376c and over-expressed Hasa- mir- 326 and Hsa-mir-143 relative to BRCA-; p<0.05.

Using Coremine data mining linking genes and diseases differentially expressed circulating miRs are linked to tumor suppressor TGFbeta/SMAD3.

Conclusions The early onset of breast cancer in BRCA mutant patients may recapitulate the pro-oncogenic effects of TGF-β. The context dependent SMAD3 binding & tumor suppression TGF-β effects are abrogated in BRCA mutant patients. TGF-β/Smad3 tumor-suppressor signature suppresses local inflammation in the tumor microenvironment.
### Abstracts

**P5**

**SYSTEMIC MASTOCYTOSIS PRESENTING AS CARDIAC TAMPODANE WITH CD25+ PERICARDIAL MAST CELLS**

VK Sukrithan, JN Salamon, G Berulava, NE Sibinga, AK Verma. Internal Medicine, Albert Einstein College of Medicine, Bronx, NY, United States; Cardiology, Albert Einstein College of Medicine, New York City, NY, United States; Hematology and Oncology, Albert Einstein College of Medicine, New York City, NY, United States; Department of Pathology, Montefiore Medical Center, Albert Einstein College of Medicine, New York City, NY, United States

**Purpose of Study** Case.

**Methods Used** Descriptive.

**Summary of Results** A 59 year old man with a history of lymphadenopathy, presented with shortness of breath and pleuritic chest pain since three days. A hyperpigmented maculopapular rash with urticaria was present along with multiple syncopal episodes and chronic diarrhea. CT scan of the abdomen in 2006 revealed lymphadenopathy, hepatosplenomegaly, and osteosclerosis. Inguinal and cervical lymph node biopsies in 2006 and 2012 were negative for malignancy. In 2009, he was diagnosed with non-ischemic cardiomyopathy with an ejection fraction of 40%. Peripheral blood, lymph node, and bone marrow flow cytometry were also unrevealing. On admission, the eosinophil count on admission was 500/µL. Echocardiography showed a large pericardial effusion with impaired right ventricular filling and significant respiratory variation in transmitral flow velocity. A pericardial window was placed, with drainage of approximately 1 liter of exudative fluid. During the surgery, the patient suffered sudden hypotension requiring epinephrine infusion. Tryptase levels drawn were 115 and 154 ng/ml. Pericardial tissue showed scattered c-Kit+ and CD25+ mast cells consistent with Systemic Mastocytosis. The transient hypotension was likely due to distributive shock from mast cell degranulation. Hyperactive mast cells may have served as mediators of the inflammatory response, contributing to production of the pericardial effusion leading to tamponade.

**Conclusions** SM with tamponade.

**P6**

**CIRCULATING MICRORNA PATTERN DEFINES A BIOLOGICALLY DISTINCT BREAST CANCER PATTERN IN BLACK (B) WOMEN RELATIVE TO ONE OCCURRING IN WHITE (W) WOMEN**

I Shapira, P Daksharam, V Kremer, A Banavali, N Kopf, A Naboush, A Shih, C Mason, A Lee. Medicine, SUNY Downstate Medical Center, Brooklyn, NY, United States; The Feinstein Institute for Medical Research, Manhasset, NY, United States

**Purpose of Study** Black women with triple negative breast cancer have 46% lower survival rates attributed to differences in tumor biology. We analyzed presurgical plasma microRNA of white (W) and black (B) women with TNBC enrolled in our breast ovarian tissue bank between 2004 and 2014.

**Aims** Detect microRNA patterns in pre-surgical plasma of TNBC W or B

**Methods Used** Between 2004 and 2014 we investigated patterns of plasma miRNAs collected before, after surgery, during and after chemotherapy in 67 patients presenting for surgery for breast cancer (W=44 & B=44) and 25 age and race matched normal controls. Two-sample t-test was used for all 2-sample comparison and ANOVA followed by Benjamin Hochberg post-hoc test to compare the mean response between subject factors of interest. All tests were 2-tailed and results with a p<0.05 were considered statistically significant. Coremine was used to identify datasets in breast cancer microarray with emphasis on our differentially expressed circulating miRs.

**Summary of Results** Mean age cancer 48 (range 35–78), control 44 (range 35–67): B patients did not express over 70% of pre-surgical plasma miRs over-expressed in the W pre-surgical plasma. Black patients had lower expression of miRs: −16-5p, −484, −126, −150-5p, −142-3p, −30c-5p, −186-5p, 139-5p. Samples from white patients overexpressed miRs−126, −150-5p, −142-3p; −30c-5p, −186-5p, 139-5p compared to healthy controls. These miRs significantly suppressed in blacks p<0.05.

Coremine text mining suggests differentially regulated microRNA are involved in mitochondrial quality control and biogenesis.

**Conclusions** Deregulation in circulating miRs between B and W patients point to pathways involved in mitochondrial fission and fusion. Aberrant mitochondria biogenesis was reported as mechanism for cancer stem cell survival and detrimental to innate immunity. Such pathways could explain the lower survival seen in black breast cancer patients.
P7 POSTPARTUM DEPRESSION POSITIVE SCREEN PREDICTORS IN A PEDIATRIC ED
L Jarvis, G Badolato, K Breslin, M Goyal. Emergency Medicine, Children’s National Health System, Washington, DC, United States
10.1136/jim-2016-000080.47

Purpose of Study The World Health Organization (WHO) and Toronto Public Health (TPH) performed a systematic literature review to identify predictors for different risk categories for postpartum depression (PPD). This review did not include patients in the pediatric emergency department (PED) setting. This study determines if the predictors identified in the WHO/TPH review are associated with positive PPD screens in an urban PED.

Methods Used We performed a prospective, cross-sectional survey of a convenience sample of mothers presenting with low-acuity triage level infants ≤ six months old to a PED. We calculated frequency of positive PPD screen predictors and performed multivariable logistic regression to identify association with a positive PPD screen.

Summary of Results 121 mothers were screened for PPD during presentation to the PED with their infant; 27 (22%) screened positive. Adjusting for maternal age, race/ethnicity, and insurance status, WHO/TPH “strong” predictors of a previous history of depression (aOR 6.7; 95% CI 1.6, 28.6), a previous history of anxiety (aOR 16.1; 95% CI 2.1, 125.5), depressed mood or anxiety during this pregnancy (aOR 25.6; 95% CI 6.7, 98.2), a recent stressful life event (aOR 5.4; 95% CI 1.9, 15.2), and lack of social support (report that they did not have someone they could count on to help with the baby; aOR 6.5; 95% CI 1.6, 26.9) were significantly associated. Our study

Conclusions Results in this urban PED are largely consistent with WHO/TPH predictors of PPD developed in other settings. Understanding PPD predictors can help physicians to improve screening and identification of PPD positive mothers.

P8 CHEMOTHERAPY INDUCED IMMUNE THROMBOCYTOPENIA-AN ENTITY TO KEEP IN MIND!
P Draksharam, J Park, G Sidhu. Hematology/Oncology, SUNY Downstate Medical Center, Brooklyn, NY, United States
10.1136/jim-2016-000080.48

Purpose of Study Thrombocytopenia during chemotherapy is not always due to myelosuppression. We report an unusual case of isolated acute thrombocytopenia after oxaliplatin and irinotecan administration. We reviewed 11 reported cases to better understand the nature of the presentation and variability in response to treatment.

Case Report Patient is a 63 year old female with metastatic colon cancer treated with palliative chemotherapy with FOLFOX. Following her 14th cycle she had an episode of acute drop in platelet count to 8,000/microliter. Peripheral smear revealed no evidence of thrombotic microangiopathy. She was managed with supportive platelet transfusions with slow recovery of platelet count. Subsequently she was treated with second line chemotherapy with FOLFIRI. Following the first cycle of Irinotecan, she again had a catastrophic drop in platelets from 136,000/microliter to 6,000/microliter within 10 hours. Due to this recurrent episode, a drug mediated thrombocytopenia was suspected and work up was initiated. She was initially treated with dexamethasone without a significant response. Platelet count normalized after 7 days with supportive platelet transfusions.

Methods Used Blood was tested for drug dependent platelet antibodies by Flow Cytometry at the Platelet and Neutrophil Immunology Laboratory at the Blood Center of Wisconsin.

Summary of Results The patient’s serum showed evidence of drug dependent platelet antibodies to both oxaliplatin and irinotecan.

Conclusions Drug mediated immune thrombocytopenia is not uncommon. Time to severe acute thrombocytopenia and platelet recovery time varied post exposure of the drug. It is unclear whether steroid or IVIG administration had any effect on the platelet recovery time. Recovery from thrombocytopenia was observed in all 11 cases after the discontinuation of the insulting agent. Confirmation of the presence of drug dependent platelet antibodies against the chemotherapeutic agent by flow cytometry essential for diagnosis. This would be the first reported case of acute thrombocytopenia to two different chemotherapeutic agents in the same patient. Whether the reaction is two different mechanisms or if there is a cross reactivity between Oxaliplatin and Irinotecan has yet to be investigated.
serum biomarkers like procalcitonin may aid in the early diagnosis of sepsis and therapeutic intervention. Procalcitonin belongs to a class of molecules, called “hor-mokines,” given the hormonal origin of the protein and the inflammation-related functions of its propeptides. Procalcitonin is a potent amplifier of the inflammatory cascade. It has shown that it induces pro-inflammatory like effects on leukocytes (increased expression of surface markers), increases leukocyte-derived cytokines and also augments nitric oxide. Procalcitonin was found to be a more accurate diagnostic parameter for sepsis. A systemic review and meta-analysis revealed that procalcitonin has a mean sensitivity of 77% and specificity of 79%. Elevated level of procalcitonin was found to be a better predictor of mortality and identify patients at higher risk of adverse outcomes. Procalcitonin is found to be superior to C-reactive protein, TNF-α, Interleukins and Lactate levels in terms of accuracy at identifying sepsis and assessing the severity of sepsis. Implementation of a procalcitonin-guided antibiotic therapy in clinical setting was associated with a reduced duration of antibiotic therapy in septic patients without compromising clinical or economical outcomes. Conclusions Procalcitonin has been proved to be more reliable biomarker in diagnosing sepsis and predicting clinical outcome. Integrating use of procalcitonin in the early golden hours of sepsis diagnosis and antibiotic stewardship program would be beneficial.

This review identified the association of procalcitonin and sepsis. There is still a need for better understanding of how procalcitonin fits in the immune response, therefore further studies should be towards exploring the immunological role of procalcitonin in sepsis.

**P10**

**IBRUTINIB ASSOCIATED AUTOIMMUNE HEMOLYTIC ANEMIA**

S Datla, P Draksharam, G Sidhu. Hematology Oncology, SUNY Downstate Medical Center, Kew Gardens, NY, United States

10.1136/jim-2016-000800.50

**Purpose of Study**

Autoimmune hemolytic anemia (AIHA) is a common phenomenon in Chronic lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) accounting for about 4–7% of cases. AIHA is commonly associated with certain conventional chemotherapy agents used in CLL/SLL. Ibrutinib, bruton tyrosine kinase inhibitor is category 1 indication for high risk (del 17p) and relapsed/refractory CLL. Literature review reports 11 cases of Ibrutinib associated AIHA.

We report a case of AIHA precipitated by Ibrutinib in an high risk CLL patient, with prior history of AIHA.

**Methods Used**

Patient is an 81 year old black man diagnosed with asymptomatic Stage I CLL (del 17p) in 2010 and was on active surveillance. He developed AIHA in 2012, with good response to steroids and Rituximab. Subsequently he received 8 cycles of rituximab for symptomatic CLL with resolution of symptoms. In 9/2014, noted to have progression of disease with worsening B symptoms, leukocytosis and lymphadenopathy. He was started on Ibrutinib 420 mg PO daily with regression of lymphadenopathy within 3 weeks of therapy, but presented with symptomatic anemia with hemoglobin of 3 gm/dl, positive direct Coomb’s test, elevated reticulocyte count and LDH consistent with AIHA. WBC elevated at 360 K/uL from baseline of 130 K/uL and hemoglobin fell to 3 g/dl from 10 g/dl since Ibrutinib was initiated. Ibrutinib was held and patient received high dose prednisone followed by IVIG and cautious transfusion with minimal improvement in hemoglobin. Hemoglobin slowly up trended with weekly Rituximab and high dose steroids and remained stable around 10 gm/dl after 4 weeks of Rituximab. Ibrutinib was subsequently restarted with overall clinical improvement.

**Summary of Results**

In our patient, occurrence of AIHA falls in between 2–4 weeks as other reported cases suggesting that Ibrutinib could be a likely precipitating factor.

**Conclusions**

Review of data, reveals that 22% of patients had history of AIC prior to Ibrutinib, however occurrence of AIHA on Ibrutinib seems to be less common (0.7%). Mechanism of action of Ibrutinib associated cytopenias remains unclear. It was hypothesized that it may be due to IL-2 induced kinase inhibition by Ibrutinib, and needs further investigation.

**P11**

**ADULT T CELL LYMPHOMA (ATL) MASQUERADING AS FACIAL NERVE PARALYSIS**

N Mukhi,1 J Park,2 P Draksharam,1 G Sidhu,1 I Shapija1.1 Hematology/Oncology, SUNY Downstate Medical Center, Glen Oaks, NY, United States; 2Internal Medicine, SUNY Downstate Medical Center, Brooklyn, NY, United States

10.1136/jim-2016-000808.51

**Purpose of Study**

ATL is a rare and aggressive peripheral T-cell neoplasm characterized by clonal human T-cell lymphotropic virus type-1 (HTLV-1) proviral DNA integration with host T lymphocytes. These patients commonly present with lymphadenopathy, skin rash, fever, fatigue or altered mental status. The prevalence of CNS disease varies from 3 to 50% and is always in the presence of systemic disease. Isolated cranial neuropathy as a presenting symptom has not been described in literature.

**Methods Used**

Retrospective chart review and review of literature.

**Summary of Results**

49 year old Caribbean male presented with 2 month history of left sided headache, 5 weeks of right sided jaw numbness and pain which progressed to contralateral side. He was now unable to smile and had food falling from the side of his mouth. He denied fever, fatigue, night sweats, rash, weakness or abnormal lumps. He had normal mental status and good motor strength. Facial exam reveal bilateral upper and lower facial paralysis, left lateral rectus palsy and horizontal gaze diplopia. Rest of the physical exam was unremarkable. Labs revealed WBC of 6 k/mm3 with normal differential, HB 16.5 gm/dl and platelets 238 k/mm3. Complete metabolic profile and peripheral smear was normal. MRI Brain showed irregular, fusiform enhancement of left trigeminal nerve, bilateral facial and abducent nerves. CSF flow cytometry showed clonal CD4+
CD25+ T cell population. HTLV-1 serology was reactive. Left infraorbital nerve biopsy confirmed involvement with ATL. CT Chest/abdomen/pelvis did not reveal enlarged lymphadenopathy. He was started on treatment with EPOCH and twice weekly intrathecal methotrexate for 4 months with clearance of CNS fluid. His jaw pain and vision improved but facial nerve paralysis persisted. He developed local relapse four months after treatment and was treated with high dose methotrexate for 5 cycles. Ultimately his performance status deteriorated and he succumbed to the disease progression.

Conclusions This case illustrates the unique presentation of this disease and gives an insight on one treatment approach. This patient achieved remission with our approach of aggressive chemotherapy with intrathecal methotrexate although the duration of remission was short lived.

Prior to chemotherapy, both groups had a mean leukocyte count of $6.6 \times 10^9/L$ and $6.8 \times 10^9/L$ and a mean platelet count of $313,000/mm^3$ and $255,000/mm^3$ respectively. At 9 months mean leukocyte counts were $6.3 \times 10^9/L$ and $5.4 \times 10^9/L$ and the mean platelet counts were $186,000/mm^3$ and $170,000/mm^3$ respectively. At 24 months, the mean leukocyte counts were $6.7 \times 10^9/L$ and $5.7 \times 10^9/L$ and the mean platelet counts were $220,000/mm^3$ and $196,000/mm^3$ respectively.

Conclusions When given on day 4 of a 14 day cycle, there was no effect of pegfilgratim on complete blood counts in this small retrospective cohort study; finding a more subtle effect would require a larger sample size.

**P12 UNABLE TO BE PUBLISHED**

10.1136/jim-2016-000080.52

Unable to be published.

**P13 THE EFFECT OF PEGFILGRASTIM ON COMPLETE BLOOD COUNT IN COLORECTAL CANCER PATIENTS TREATED WITH FOLFOX OR FOLFIRI CHEMOTHERAPY**

V Kremer,1 I Shapira,2 A Leaf,1 1Hematology/Oncology, SUNY Downstate Medical Center, Brooklyn, NY, United States; 2Hematology/Oncology, New York Harbor Healthcare System, Brooklyn Campus, Brooklyn, NY, United States

10.1136/jim-2016-000080.53

**Purpose of Study** In both FOLFOX and FOLFIRI regimens used for colorectal cancer, the 5-FU is infused over 46 hours every 14 days. Given the 10–20% risk of neutropenic fever, these regimens may be given with pegfilgratim support. There is evidence to support its use for 21 day cycles, but no phase III trials demonstrating its efficacy and safety for regimens given every 14 days, a potential concern, given the hypothesis that the hematopoietic stem cells mobilized by pegfilgratim into the peripheral blood may undergo cell cycle arrest, apoptosis and death while under effect of chemotherapy. Pegfilgratim regulates the proliferation, differentiation, and survival of the myeloid lineage. It mobilizes hematopoietic progenitor cells in the peripheral circulation, has a long half-life, and is given on day 4 of 14-day infusional 5-FU based regimens. Given the fact that cytotoxic chemotherapy is administered on day 11 after pegfilgratim, we performed a retrospective study evaluating the correlation between decrease in complete blood count and chemotherapy administered at 11 day intervals after pegfilgratim.

**Methods Used** The medical records of colorectal cancer patients were reviewed from 2003–2013. Data collected included age, stage, ethnicity, complete blood count, chemotherapy, and use of pegfilgratim.

**Summary of Results** Data from 50 eligible charts was collected. Twenty one patients were treated with chemotherapy and pegfilgratim, 29 patients had chemotherapy alone.

**P14 DOXYCYCLINE: A RARE CAUSE OF DRUG INDUCED PANCREATITIS**

M Pournemeta,1 H Vird,1 D Yoon,2 R Islam,4 A Ras,3 Z Rahman.1 1Internal Medicine, ETSU Quillen College of Medicine, Johnson City, TN, United States; 2Radiology, Mount Sinai St. Luke’s and Mount Sinai Roosevelt Hospitals, New York, NY, United States; 3Green Templeton College, University of Oxford, Oxford, United Kingdom; 4Department of Medicine, Mayo Hospital, King Edward Medical University, Lahore, Pakistan

10.1136/jim-2016-000080.54

**Purpose of Study** Drug-induced pancreatitis (DIP) is a rare clinicopathologic entity. We report a 58-year-old female who developed DIP secondary to administration of doxycycline.

**Methods Used** A 48 year old female with a history of hypertension presented to the hospital with complaints of nausea/vomiting, right upper-quadrant gnawing abdominal pain, 8/10 in intensity with radiation to the back. She denied exacerbating factors, use of alcohol, tobacco and drug. Patient also denied diarrhea, constipation and changes in skin or stool color. On examination patient was hypertensive (155/95) with a heart rate of 102. She had epigastric/right upper quadrant tenderness on superficial palpation, hypoactive bowel sounds without any palpable organs, rebound tenderness or rigidity. Serum lipase was elevated at 2508 IU/L, negative pregnancy and insignificant urinalysis findings. Liver function tests, lipid panel, chemistry panel and hematologic panel were within normal limits. Radiologic investigations with abdominal ultrasound depicted mild proximal dilatation of the common bile duct with smooth tapering of the duct distally indicating status post-cholecystectomy. Contrast enhanced computed tomography scan revealed mild enlargement of the body of the pancreas with adjacent peripancreatic fatty infiltration consistent with acute pancreatitis. Upon further questioning patient explains recent diagnosis (7 days) of tibial orthopedic hardware infection as she was prescribed doxycycline 200 mg twice a day in anticipation of irrigation of infected site. After confirmation, and discontinuation of doxycycline, our patient recovered and has been disease-free for over a month.

**Summary of Results** Drug-induced pancreatitis is uncommon etiology of acute pancreatitis, which is responsible for 0.1%–2% of all the acute pancreatitis cases. Among adverse drug reactions, pancreatitis is often-ignored because of the difficulty in implicating a drug as its cause.
Conclusions In our vastly evolving pharmacotherapy world, DIP should be included in the differential of idiopathic pancreatitis, especially after other common causes have been ruled out.

**P15** RELAPSING EROSI VE POLYARTHRITIS ASSOCIATED WITH HIDRADENITIS SUPPURATIVA

AG Adiga, JS Pixley. Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, TX, United States

Purpose of Study Hidradenitis Suppurativa (HS) is a chronic disorder involving apocrine glands characterized by comedo like follicular occlusion and a chronic relapsing inflammation; sinus tracts and scarring. We observed a case of HS in a young African American (AA) male with relapsing polyarthritis.

Methods Used The patient first developed HS as a teenager and then arthritis 10 years later. On this presentation he had multiple nodular skin lesions, predominately in intertriginous areas in the axilla and inguinal area; few of them presenting as draining pustules which had increased in size and number as well as generalized arthritis. This occurs 1–2 times yearly subsiding in association with antibiotic treatment. Physical examination was notable for generalized suppurate nodules chronic scars and sinuses. Joint examination revealed generalized polyarthritis with effusions in ankles, knees and elbows. Laboratory evaluation revealed marked inflammation. Autoantibody studies were negative. Radiographs revealed demineralization, erosions including the distal interphalangeal joints with suggestion of pencil/cup deformity in an asymmetric manner. All cultures were negative. Urine Chlamydia and Neisseria polymerase chain reaction testing was also negative.

Summary of Results Musculoskeletal association with HS has been reported. Most note an association of skin flares and that it tends to occur years after the onset of skin disease. Most reports are anecdotal. We identified one multicenter analysis. The pattern of disease described resembles the spondyloarthopathy manifestations including sacroiliitis, dactylitis, inflammatory back pain and enthesitis. Our patient’s findings were consistent with the limited literature available.

Conclusions In conclusion, we propose that inflammatory spondyloarthopathy may be a complication of HS.

**P16** CARDIAC ARREST AS A CONSEQUENCE OF AIR EMBOLISM STATUS POST CT-GUIDED LUNG BIOPSY

M Pourmorteza,1 G Murtaza,1 P Mamdouhi,1 Z Ur Rahman,1 P Sethi,2 TK Paul2. 1Internal Medicine, ETSU Quillen College of Medicine, Johnson City, TN, United States; 2ETSU, Department of Cardiology, Johnson City, TN, United States

Purpose of Study CT-guided transthoracic lung biopsy (CTLB) is a widely used procedure for the diagnosis of pulmonary lesions. Complication of air embolism has an incidence of 0.02%–0.06%. We report a fatal case of air embolism in the left atrium as a consequence of CTLB.

Methods Used A 82 years old white female who presented to the radiology department for further evaluation of a recently diagnosed right lung mass. Shortly following CTLB she became unresponsive and developed cardiopulmonary arrest. Cardio-pulmonary resuscitation (CPR) was performed according to ACLS guidelines. She was successfully resuscitated and admitted to the ICU. CT chest was performed immediately after resuscitation which showed frothy air dense material in the left atrium and one of the right pulmonary veins suggesting a Broncho venous fistula with air embolism. Patient was subsequently sent to hyperbaric oxygen chamber which she tolerated well. A repeat CT chest and head failed to depict any evidence of air embolism. She was successfully weaned from the mechanical ventilation and extubated the following day.

Summary of Results Air embolism following CTLB has a reported incidence of 0.02 to 0.06 but has catastrophic consequences if diagnosis is not made in a timely manner. The amount of air entry into the system is directly proportional to the severity of the patients symptoms. The mechanism of air entry in our patient was secondary to iatrogenic bronchovenous fistula.

Conclusions Despite such rarity and fatal complication, clinicians should be aware of systemic air embolus after lung biopsy and be ready to provide emergent management for the treatment of the patient.

**P17** PNEUMOMEDIASTINUM A RARE COMPLICATION OF COLONOSCOPY POLYPECTOMY SUCCESSFULLY TREATED WITH CONSERVATIVE MANAGEMENT

C Rives,1 M Pourmorteza,1 E Carter,2 M Young2. 1Internal Medicine, East Tennessee State University, Johnson City, TN, United States; 2Gastroenterology, East Tennessee State University, Johnson City, TN, United States

Purpose of Study Colonoscopies are a relatively safe and are associated with few complications. We present a rare case of post-colonoscopy polypectomy resulting in a pneumomediastinum and subcutaneous emphysema.

Methods Used An 84 year old male with a history of colonoscopy with polypectomy the day prior was admitted
due to a syncopal episode. The only complaint was a small amount of dark red blood per rectum. On examination vital signs were stable, the patient appeared pale with dry membrane mucosa, abdominal and pulmonary exam were benign, labs were concerning for a Hgb 6.9 g/dl. Chest X-ray depicted free air beneath the retroperitoneum, computed tomography demonstrated pneumoretroperitoneum, pneumomediastinum and subcutaneous emphysema. Visceral angiogram failed to demonstrate any source of active bleeding. Due to the overall stable condition of the patient conservative management with prophylactic zosyn and transfusion of 2 units of packed red blood cells was initiated. Patient was discharged 5 days after admission with stable respiratory and hemodynamic signs.

Summary of Results Diagnostic colonoscopies are relatively safe procedures with the most common complications being bleeding and perforations, with an incidence of less than .2%. Though perforations are rare they are associated with a high mortality and morbidity. Causes of perforation can be due to excessive insufflations, instrumental trauma and usually present with intra-abdominal free air but rarely with a pneumomediastinum. A pneumomediastinum is the presence of free air within the mediastinum and in our case was due to a micro-perforation from a colonic polypectomy. The colonic wall defect allowed free air into the retroperitoneum, which spread along the fascial planes and entered the mediastinum and subcutaneous tissues. The most sensitive test for pneumomediastinum is computed tomography and extra-pulmonary causes of pneumomediastinum can be successfully treated conservatively with rest and antibiotics.

Conclusions Though complications from polypectomies are rare, they can be associated with a high morbidity and mortality but rarely associated with pneumomediastinum and in certain stable patients can be treated with conservative management.

Laboratory results consistent with hemolytic anemia with Hb 5.6 g/dl, direct coombs positive, elevated reticulocyte count, LDH and low haptoglobin. Initial RF, ANA, and all infectious work up including HIV were normal. She was transfused cautiously, with inconclusive LN and bone marrow bx. Patient left hospital against medical advice.

She presented two days later with altered mental status (AMS) and hypotension. CT head and Lumbar puncture were negative. Hypotension responded to fluids, but no response in AMS. Repeat ANA, AntiSSB, AntiSm, AntiRNP, and Antihistone antibodies were positive. Patient met diagnostic criteria for SLE and was subsequently treated for lupus cerebritis with pulse steroids, with moderate improvement in mental status. Repeat LNBX revealed reactive lymphadenitis with features of MCD, HHV8 negative. Patient was treated with IL-6 inhibitor Siltuximab, with significant improvement in mental status.

Summary of Results MCD is a rare angiolymphoproliferative disorder of unclear etiology. Most cases occur in middle aged men and are associated with immunosuppression where as SLE is common in women of child bearing age. Reported cases of MCD in association with SLE are common in immunocompetent young women. Our patient is a young woman, HIV/HHV8 negative with good response to Siltuximab, favoring MCD.

Conclusions It is unclear whether this finding of MCD and SLE represents an overlap or a pure association. However, this phenomenon needs further investigation.

**Abstracts**

**P18** MULTIPLE DIAGNOSIS OR CONTINUUM OF DISEASE: MULTICENTRIC CASTLEMAN’S DISEASE
S Datla,1 K Parker,2 L Robert,1 N Soloman1.1 Hematology Oncology, SUNY Downstate Medical Center, Kew Gardens, NY, United States; 2Rheumatology, SUNY Downstate Medical Center, Brooklyn, NY, United States

10.1136/jim-2016-000080.58

**Purpose of Study** Multicentric Castleman’s disease (MCD) is a rare lymphoproliferative disorder characterized by peripheral lymphadenopathy (LAD), hepatosplenomegaly (HSM), and B symptoms. It is associated with HIV and HHV8 infection.

We report a case of young woman presented with B symptoms, workup suggestive of lupus but lymph node biopsy (BX) was consistent with MCD. Association of SLE with MCD is rare. We report this case to increase awareness of this potential diagnostic and therapeutic dilemma.

**Methods Used** Patient is a 27 yr old black woman presented with malaise, fevers, cough, weight loss, arthralgia, alopecia, numbness of extremities and Raynaud’s phenomenon. Patient had skin tightness around the mouth, telangiectasia, digital ulcers, HSM, pitting edema, diffuse LAD and moderate pericardial effusion.
due to interactions between genes, environment, and abnormalities of the adaptive immunity. T cells, polyclonal B cell activation, hypergammaglobulinemia, autoantibodies and immune complexes. Asthma and autoimmune disease are associated with increased incidence of ANA's suggesting the disease may have an autoimmune basis.

Our case describes a 49 year old man with SLE, diagnosed with Raynaud’s, childhood asthma, mental retardation, depression, pancreatitis and referred for a generalized rash sneezing, and nasal congestion. Physical exam revealed normal vitals, bald head, diffuse facial skin freckles erythematous nasal turbinates, dermatitis of the lower extremity, normal cardiac finding, no wheezing or Raynaud’s, + abdominal tenderness, sIgE testing was performed for allergic rhinitis.

Conclusions This interesting case illustrates a clear link with symptoms of allergic rhinitis, asthma and SLE.
### Author index

The number next to the author indicates the page number, not the abstract number.