A REDUCTION IN EJECTION FRACTION DURING STRESS WITHIN THE NORMAL RANGE WITH GATED SPECT IMAGING IS NOT ASSOCIATED WITH INCREASED MORTALITY

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Purpose of Study: We sought to establish the prognostic significance of a stress induced fall in ejection fraction ≥10 in patients with normal resting baseline systolic function whose ejection fraction (EF) falls with stress but remains within the normal range.

Methods Used: 5,600 patients underwent gated, nuclear myocardial SPECT stress testing over a period of 6 years. Patients were followed prospectively and mortality assessed from the centralized Veterans Affairs electronic medical record (CPRS-VISTA). All cause mortality was compared between patients with normal systolic function where a post stress EF remained unchanged and those patients whose post stress EF remained within the normal range but decreased by ≥10.

Summary of Results: A total of 1441 patients had a normal resting systolic function that remained unchanged with stress while 139 patients demonstrated a stress induced fall in EF ≥10 while still remaining within the normal range (≥46%). Both groups were similar with respect to age (63 ± 14; 65 ± 12 yrs), weight (197 ± 46;199 ± 52 lbs), and resting blood pressure (128 ± 20; 128 ± 20 mmHg; p=ns). Resting EF was significantly higher (59 ± 8%; 68 ± 7%; p < 0.05) in those pts where stress induced EF fall of ≥10 while still remaining in the normal range. During a follow up period of 6 yrs survival was 94% at 1 yr, 85% at 3 yrs, & 78% at 5 yrs with no differences between the two groups.

Conclusions: In patients with normal resting systolic function a stress induced fall in EF ≥10 when remaining within the normal range does not have an adverse effect on survival.

VITAMIN D DEFICIENCY AS A RISK FACTOR FOR ALLERGY IN THE US USING THE NHANES SURVEY

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Purpose of Study: Vitamin D has been reported in very high rates in US population and implicated in various diseases such as diabetes, high blood pressure, cardiovascular disease, many cancers and in immune system dysregulation. Our hypothesis is that low vitamin D has been implicated with increased incidence of various types of allergic conditions.

Methods Used: The National Health and Nutrition examination survey (NHANES) 2005Y2006 as a cross sectional survey done on the noninstitutionalized population of the United States by the Centre for Disease Control and Prevention and National Centre for Health Statistics consists of an extensive interview done at home and an examination done at a mobile center. An allergy questionnaire provided interview data on self-reported allergic diseases including hay fever, allergies and eczema. The data was collected using the question BHas the doctor or other health professional ever told that you have allergies and using the lab parameter vitamin D less than 10ng/ml. The data was analyzed by logistic regression with SAS version 9.1 (Cary, NC) using the PROC SURVEY methods.

Summary of Results: Out of 10348 people who participated in 2005Y2006 NHANES survey, our final sample consisted of 4979 people after deleting people less than 20 years and those with missing values. The vitamin D deficiency was positively correlated with prevalence of allergies (odds ratio of 1.37, 95% CI of 1.14 to 1.69). After adjusting the model for age, gender, race, smoking, alcohol, and educational status odds ratio still remained significant (OR of 1.34, 95% CI of 1.10 to 1.63). A positive correlation was noted with rashes, sneezing and sinus infections.

Conclusions: Our study showed a positive association between vitamin D deficiency and prevalence of allergies. Based on the magnitude of deficiency and its association with other diseases a careful consideration has to be given in educating the general population about the vitamin D intake. 1,25(OH)(2)D(3) can potentiate the efficacy of allergen immunotherapy used for allergic rhinitis therapy effecting regulatory cytokines IL-10 and TGF beta. Supplementation can result in correction of defects in cathelicidins in the innate immune system of atopic subjects related to eczema. More research is needed to confirm this relationship and to elucidate its effects on the immune system.
5 RELATIONSHIP BETWEEN LEFT VENTRICULAR MASS AND AORTIC VALVE CALCIFICATION: THE MULTI-ETHNIC STUDY OF ATHEROSCLEROSIS

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Purpose of Study: Aortic valve calcification (AVC) occurs during the early stages of valve remodeling, frequently before the development of hemodynamic valve obstruction. Data suggest that left ventricular hypertrophy, widely considered a compensatory consequence of aortic stenosis (AS), may be associated with calcific aortic valve disease (CAVD) in the absence of AS.

Methods Used: 5,042 subjects aged 45-84 years underwent cardiac magnetic resonance imaging and computed tomography (CT) within the Multi-Ethnic Study of Atherosclerosis (MESA). The relationship of baseline percent of predicted left ventricular mass (LVM; standardized for gender, height, and weight) to the prevalence, severity, and incidence of AVC was determined by regression analysis.

Summary of Results: AVC was prevalent in 631 subjects at baseline. An additional 227 subjects developed incident AVC at follow-up (median 3.1 years later). After adjustment for age, gender, body mass index, demographics, study site, antihypertensive therapy, statin use, diabetes, smoking status, blood pressure, and cholesterol levels, LVM was positively associated with AVC prevalence (prevalence ratio=1.106 [95%CI 1.03, 1.17]; p=0.0005; all results reported per 10% increase) and severity (risk difference = 1.15 [95%CI 1.09, 1.22]; p=0.0001) at baseline. In those without AVC at baseline, LVM was associated with the development of AVC (relative risk=1.17 [95%CI 1.05, 1.31]; p=0.005).

Conclusions: In the diverse MESA cohort, LVM was associated with prevalence and severity of AVC. An association between baseline LVM and incident AVC suggests that increased left ventricular mass may precede CAVD. Further study is needed to determine the mechanisms responsible for this association and evaluate its impact on patient outcomes.

6 A PROSPECTIVE STUDY AND COST ANALYSIS OF MALARIA TESTING AND EMPIRIC TREATMENT

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Purpose of Study: To compare the cost of empirical treatment for all clinically diagnosed with malaria to the costs of testing all and treating only those with positive Giemsa thick blood smears at a major medical center in southwestern Nigeria. We also assessed the test performance of the Leishman thin blood smear (compared to Giemsa) since the Leishman is often used in Nigeria to diagnose malaria.

Methods Used: All patients in our study with the clinical diagnosis of malaria received free Leishman thin smear, Giemsa thick (diagnosis) and thin (differential) smears, and antimarial treatment. Clinical malaria was diagnosed per medical center doctors’ judgments involving symptoms of malaria. Direct patient costs (drugs and smears) were calculated from the medical center’s charges. The cost for the pediatric treatment regimen of artesunate 6–9 tablets and amodiaquine suspension was 660 naira (N660=US$4.41 in mid-2009). Adults were given two treatment options: option one (12 tablets of artesunate and 3 tablets of sulfadoxine pyrimethamine) cost N610 ($4.07) and option two (12 tablets of artesunate and 8 tablets of amodiaquine) cost N680 ($4.54).

Summary of Results: Doctors diagnosed and treated 304 patients (170 adult and 134 pediatric) with clinical malaria. Of the 304 tests, Giemsa thick smears were positive in 115 (38%), while and Leishman thin smear were positive in 52 (17%). The sensitivity of the Leishman was 52/115=45%.
and the specificity is 189/189 = 100%. The patient cost of one Giemsa smear was N550.00 ($793.65) and their empiric treatment cost N884.40 ($598.84). The cost of testing all and treating only Giemsa positive adults was N1209.50 ($806.61) for option one and N124100.00 ($827.61) for option two. The respective costs for empiric treatment of all adult patients was N103700.00 ($691.57) and N115600.00 ($770.93).

**Conclusions:** In southwestern Nigeria, the most cost-effective approach to malarial management was empiric treatment, though many uninfected children and adults will receive antimalarial drugs. The widely used Leishman thin smear was insensitive compared to the Giemsa smear which should be the preferred diagnostic approach.

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**7 OVERCOMING HETEROGENEITY IN PEDIATRIC ASTHMA: TOBACCO SMOKE AND ASTHMA CHARACTERISTICS WITHIN PHENOTYPIC CLUSTERS**

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**Purpose of Study:** Asthma is a heterogeneous syndrome comprised of multiple poorly defined subgroups with variable disease expression and response to environmental exposures. We sought to define homogeneous phenotypic clusters within pediatric asthma and to determine overall and within-cluster associations between environmental tobacco smoke (ETS) exposure and asthma characteristics.

**Methods Used:** A combined hierarchical-k-means cluster analysis of principal component variables was used to define phenotypic clusters within a cohort (n = 100) of 6 to 20 year-old urban and largely minority subjects with asthma.

**Summary of Results:** Phenotypic cluster analysis defined three independent clusters within the cohort. Three individuals grouped into a very small fourth cluster and were ultimately excluded. Several characteristics defined the three remaining clusters. Of note, patients in Cluster 1 (n = 53) showed an abundance of nasal neutrophils (46%) relative to Clusters 2 and 3 (20% and 28%; P = 0.025). Patients in Cluster 2 (n = 23) were predominantly female (61% versus 26% and 48% in clusters 1 and 3, respectively; P < 0.001) and higher body mass index (BMI) percentile (90% versus 62% and 66%; P < 0.001) with later-onset asthma (7 years versus 2.0 and 1.2 years; P = 0.003). Patients in Cluster 3 (n = 21) had an allergic phenotype with an increased proportion of nasal eosinophils (65% versus 35% and 58% in clusters 1 and 2, respectively; P = 0.007) and lower mean Asthma Control Test (ACT) scores (16.1 versus 22.4 and 20.6; P < 0.001). Within-cluster regression analysis revealed several significant associations that were not present in the overall cohort. For example, ETS exposure was associated with a significant reduction in the bronchodilator-induced change in FEV1 (Beta Coefficient = -3.23 [95% CI: -6.10 to -0.35]; P = 0.029) within Cluster 1 and a significantly increased National Asthma Education and Prevention Program (NAEPP) severity classification (B = 1.12 [0.11 to 2.13]; P = 0.030) within Cluster 2.

**Conclusions:** Clustering techniques were used in this study to define more homogeneous subgroups allowing for the detection of otherwise undetectable associations between ETS and asthma characteristics.

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**8 PRIMARY CARE FOLLOW-UP AFTER EMERGENCY DEPARTMENT VISITS FOR LOWER RESPIRATORY ILLNESSES AMONG A DISADVANTAGED URBAN PEDIATRIC POPULATION**

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**Purpose of Study:** To determine and compare FU rates with PCPs after ED discharge among disadvantaged urban pediatric patients with lower respiratory illnesses.

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**9 A RETROSPECTIVE STUDY TO EVALUATE THE IMPACT OF ERYTHROPOIETIN STIMULATING AGENTS ON CARDIOVASCULAR OUTCOMES INDEPENDENT OF THEIR EFFECT ON HEMOGLOBIN**

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1Division of Cardiology, Howard University Hospital, Washington DC, DC 2Department of Nephrology, Washington Hospital Center, Washington, DC 3Center for Minority Health Services Research, Howard University, Washington, DC 4Department of Internal Medicine, Howard University Hospital, Washington, DC.

**Purpose of Study:** This retrospective cohort study was designed to examine if patients with chronic kidney disease who have received erythropoietin stimulating agents (ESA’s) have an additional cardiovascular advantage compared to those who have not, despite having similar hemoglobin values in target range of 11–12 mg/dl.

**Methods Used:** A retrospective cohort study of a random sample of patients followed within the primary care system of an urban pediatric tertiary care center and discharged from its ED with an isolated diagnosis of acute asthma (ages 2–6y and 7–12y), bronchiolitis (0–24m), croup (6m–6y), or pneumonia (0–6y) during 2007. Data collected included driving distance from patient’s home to PCP’s office and explicitness of written ED discharge instructions in specifying FU. Rates of PCP FU within 7d and 30d were determined with electronic records.

**Summary of Results:** Data from 467 study subjects are presented in the table. The odds of FU significantly increased for each 1 year increase in age [OR 1.05 (95% CI 1.02–1.08)] while they significantly increased if explicit discharge instructions were provided [OR 1.67 (95% CI 1.06–2.6)].

**Conclusions:** Rates of FU were low and positively associated with younger age and receiving explicit discharge instructions. The odds of FU were significantly higher for patients with acute pneumonia (0–6y) than those with an acute exacerbation of chronic asthma (2–6y).

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**Table.**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Asthma 2-6y</th>
<th>Asthma 7-12y</th>
<th>Bronchiolitis 0-24m</th>
<th>Croup 6m-6y</th>
<th>Pneumonia 0-6y</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
<td>N (95% CI)</td>
</tr>
<tr>
<td>4.2 (3.1–4.8)</td>
<td>9.5 (8.5–10.1)</td>
<td>0.6 (0.5–0.7)</td>
<td>1.6 (1.4–1.9)</td>
<td>2.3 (1.7–2.7)</td>
<td></td>
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</tbody>
</table>

**Adjusted OR of FU within 7d (95% CI):**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.05 (1.02–1.08)</td>
<td>1.67 (1.06–2.6)</td>
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</table>

**Conclusion:** Adjusted for age, insurance type, distance from patient’s home to PCP, and provision of explicit discharge instructions. **Not adjusted for age.**
for a mean duration of one and a half years to determine the occurrence of the primary endpoint.

Summary of Results: There were 21 (28.8 percent) hospitalizations for cardiovascular events in patients who did not receive ESA and 8 (20 percent) hospitalizations for cardiovascular events in the ESA group (unadjusted p value 0.56). There were no deaths in either group during the study period. After multivariable analysis adjusting for baseline differences in medication use there was a relative risk reduction in hospitalizations in the ESA group by 62 percent compared to patients who did not receive ESA (RR 0.38; 95% CI 0.16–0.94; p value <0.05).

Conclusions: We conclude that the use of ESA’s decreases hospitalizations for cardiovascular adverse events in patients with chronic kidney disease (pre-dialysis) independent of their effect on hemoglobin and hematocrit.

Methods Used: We prospectively studied 101 consecutive patients hospitalized with the primary diagnosis of heart failure who had ejection fraction of 50% or greater. CA125 levels were measured by electrochemiluminescence immunoassay within 72 hours of hospitalization. The end point of the study was death or rehospitalization for heart failure, whichever came first.

Summary of Results: The mean CA125 level was 40.4 U/mL. The CA125 threshold value derived from the receiver operation characteristic curves for the prediction of the prespecified end point was 60 U/mL. Over the mean follow-up period of 8 months, 57.1% of patients who had CA125 level ≥ 60 U/mL reached the study end point, compared with 25% of patients with CA125 level < 60 U/mL (log-rank P = 0.013). Using Cox proportional hazards modeling, CA125 level was associated with increased risk of death/ rehospitalization for heart failure (hazard ratio, 3.14; 95% confidence interval, 1.21–8.16, P = 0.019).

Conclusions: The present study has shown prognostic significance of CA125 levels in patients with heart failure and preserved ejection fraction.
asthmatic airways may not be mediated by inflammation as previously thought but rather intrinsic to the airway epithelium. The goal of the current study was to define the intrinsic inflammmogenic and regenerative properties of asthma and normal bronchial epithelium.

**Methods Used:** Human primary differentiated bronchial epithelia were mechanically scrape-wounded in GC-free bromoeeoxyuridine (BrdU)-containing medium. Epithelia were pulsed with dexamethasone (DEX) (0 or 20nM) for 2 hours prior to wounding and daily over the ensuing 48 hours. Wound healing, inflammation, and regeneration were analyzed by microscopy and/or flow cytometry.

**Summary of Results:** Normal (n = 3) and asthmatic (n = 3) epithelia were indistinguishably quiescent at baseline. Following wounding, marked differences became apparent. Wounded asthmatic epithelia secreted more basolateral IL-1β, IL-10, and TGF-β1 (<0.001 < P < 0.024) than normals and showed 50% fewer mitotically-active (BrdU+) cells (mean=SEM: 0.27 ± 0.03% vs. 0.56 ± 0.07% of total cells; P = 0.02). Asthmatic cells were dys synchronously distributed among the cell cycle phases (G1/GO:52.1 ± 10, S:25.4 ± 4.2/M:23.7 ± 7% vs. 71.1 ± 12.2, 17.2 ± 2%). Accordingly asthma epithelia regenerated less efficiently than normals (wound area reduction=51.3 ± 5.6% vs. 78.6 ± 7.7%; P = 0.013). DEX-treatment of wounded asthmatic epithelia normalized inflammation, mitotic activity, and wound healing.

**Conclusions:** These data, generated in an airway model lacking bone marrow-derived inflammatory cells, support the concept that asthmatic epithelium is intrinsically inflammatory. Whether this is a consequence of, or a contributor to, poorly synchronized asthmatic epithelial mitosis is unclear. However, GC treatment apparently both inhibits inflammation and restores asthmatic epithelial regeneration/mitotic synchrony.

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15 RESVERATROL EXHIBITS ANTI-INFLAMMATORY PROPERTIES BY FACILITATING CHOLESTEROL EFFLUX FROM THP-1 HUMAN MONOCYTES/MACROPHAGES

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**Purpose of Study:** Resveratrol, a plant derived polyphenol found in red wine and grapes, exerts anti-inflammatory, antioxidant, and cardioprotective effects. We hypothesized that mechanisms underlying beneficial effects of resveratrol on atherosclerosis may involve prevention of cholesterol overload, limiting macrophage foam cell formation (FCF). This study examines the effect of resveratrol on expression of proteins involved in reverse cholesterol transport (RCT) out of the macrophage and on FCF in vitro.

**Methods Used:** THP-1 monocytes/macrophages, a pertinent model of atherosclerosis, were incubated with resveratrol (50 µM, 24h) with or without addition of the inflammatory atherogenic cytokine interferon (IFN)-γ (500 U/ml). Expression of the cholesterol-metabolizing enzyme P450 27-hydroxylase (27-OHase) and ATP binding cassette transporter A1 (ABCA1). These proteins are crucial for efficient cholesterol efflux, a process that prevents foam cell formation and protects against atherosclerosis. In this study, we investigated the effect of omalizumab on expression of these RCT proteins, as well as scavenger receptor CD36 (promotes cholesterol influx) in THP-1 human monocytes and compared its effect to celecoxib.

**Methods Used:** THP-1 human monocytes (10^5 cells/ml), an established model of atherosclerosis, were incubated with dexamethasone (20 hrs, 37°C, 5% CO2) ± omalizumab (500 µg/ml and 1000 µg/ml) ± celecoxib (50µM) and ± the atherogenic cytokine interferon (IFN)-γ (500 U/ml). Expression of ABCA1, 27-OHase and CD36 message was evaluated by quantitative real-time PCR. Studies were performed in triplicate.

**Summary of Results:** In cultured THP-1 monocytes, omalizumab had a modest impact on ABCA1 and 27-OHase mRNA, but had no effect on the expression of CD36 mRNA, while celecoxib significantly changed expression of each of these proteins in an atherogenic manner. Following celecoxib exposure, 27-OHase and ABCA1 mRNAs decreased by 77.9 ± 10.38% and 64.8 ± 8.55%, respectively while CD36 increased by 37.5 ± 3.91% (100% = baseline expression in untreated THP-1). Omalizumab treatment of THP-1 monocytes (1000 µg/ml) decreased message for the 27-OHase and ABCA1 by 28.6 ± 3.77% and 27.6 ± 3.68%, respectively, while CD36 expression did not change significantly.

**Conclusions:** COX-2 inhibition may contribute to the pathological process of atherosclerosis by promoting lipid overload through effects on genes limiting macrophage foam cell formation (FCF). This study examines the effect of resveratrol on expression of proteins involved in reverse cholesterol transport (RCT) out of the macrophage and on FCF in vitro.

**Methods Used:** THP-1 monocytes/macrophages, a pertinent model of atherosclerosis, were incubated with resveratrol (50 µM, 24h) with or without addition of the inflammatory atherogenic cytokine interferon (IFN)-γ (500 U/ml). Expression of the cholesterol-metabolizing enzyme P450 27-hydroxylase (27-OHase) and the ATP binding cassette transporter A1 (ABCA1). These proteins are crucial for efficient cholesterol efflux, a process that prevents foam cell formation and protects against atherosclerosis. In this study, we investigated the effect of omalizumab on expression of these RCT proteins, as well as scavenger receptor CD36 (promotes cholesterol influx) in THP-1 human monocytes and compared its effect to celecoxib.

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**Conclusions:** COX-2 inhibition may contribute to the pathological process of atherosclerosis by promoting lipid overload through effects on genes involving in cholesterol transport, while omalizumab does not substantially affect these pathways. If reported cardiovascular and cerebrovascular risks are confirmed with omalizumab, the effect is likely by an alternate mechanism.
Posters

**P1** PRIMARY HYPERPARATHYROIDISM: A POTENTIALLY TREATABLE MEDICAL CAUSE OF PROGRESSION OF AORTIC STENOSIS. A CASE REPORT

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**Purpose of Study:** A case report and discussion to highlight the early diagnosis of primary hyperparathyroidism in patients with Aortic Stenosis.

**Methods Used:** Case study and review of current literature.

**Summary of Results:** A 65-year-old male presented to the hospital for evaluation of surgery for aortic stenosis. He was diagnosed with aortic stenosis 4 years ago after having an angiogram and echo for evaluation of coronary artery disease. His echocardiogram at that time suggested mild aortic stenosis. He subsequently had a repeat echo 4 years after the initial echo which showed severe aortic stenosis with a gradients of 137/83 mmHg (peak/mean).

Echo findings:
1. Normal LV size and function, LVEF=55%. Severe LVH
2. Severe aortic stenosis by 2D appearance and aortic valve pressure gradients, PS/M gradient of 137/83 mmHg. AVA 0.7 cm2
3. Dilated ascending aorta 4.5cm.
4. Moderate posterior mitral annular calcification.

Angiogram was essentially normal.

Routine pre-operative labs also showed calcium level of 11.7 (normal 8.5 to 10.5), were otherwise normal. Her serum cholesterol was 93 and LDL was 49.

**Hospital Course:**
Patient underwent surgery consisting of aortic valve replacement with #23 Trifecta valve replacement. Post-operatively the calcium level ranged from 9.5 to 10.5. However given the rapid progression of his aortic stenosis and calcification noted on the mitral valve, a parathyroid hormone level (PTH) was sent for evaluation of hyperparathyroidism, this was found to be elevated at 169 pg/ml (normal levels 10–60), a 24 urinary calcium level was 854 mg (normal 10–300) excluding familial hypercalciuric hypercalcemia. The patient was diagnosed with primary hyperparathyroidism and referred to endocrinology for further evaluation.

**Conclusions:** Primary hyperparathyroidism if detected and treated early can potentially prevent progression of aortic stenosis.

**P2** THE INFLUENCE OF CULTURE AND GENETICS IN THE EXPRESSION OF THE METABOLIC SYNDROME


**Purpose of Study:** The expression of the metabolic syndrome (Mets) varies depending on the culture and genetics of the nation studied. The nation more influenced by U.S.A. culture is Puerto Rico (P.R.) an Hispanic country. Coronary artery disease is the island is two fold less frequent than in the U.S.A.

**Methods Used:** We compared the incidence of coronary diseases in Mets in P.R. and U.S.A. We analyzed 169 cases and found no myocardial infarction, stroke or ventricular tachycardia.

**Summary of Results:** The incidence of Mets was 35%. Further prospective studies should be done in hospitals, which use AED routinely on high risk patients to see if it is cost effective in reducing sudden cardiac deaths.

**Conclusions:** These findings suggest that genetics and culture is an important aspect in the clinical manifestation of Mets.

**P3** PREVENTION OF IN HOSPITAL SUDDEN CARDIAC DEATH WITH THE USE OF AUTOMATED EXTERNAL DEFIBRILLATORS IN HIGH RISK PATIENTS

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**Purpose of Study:** The diagnosis of in hospital resuscitation of cardiac arrest has not improved significantly over the years. The use of automated external defibrillators (AED) in high risk patients could reduce the chances of sudden cardiac death (SCD) and minimize the associated neurological injury.

**Methods Used:** Retrospective study done in patients who had SCD in MICU and telemetry units in a community hospital for a period of one year.

**Summary of Results:** 105 patients had SCD with one patient surviving the initial resuscitation but died seven days later due to anoxic encephalopathy.

The average age of the patients who had SCD was 69 years and 95% had more than four co-morbid factors. Out of the 105 patients 35 (33.3%) had either ventricular tachycardia or ventricular fibrillation before cardiac arrest and the rest had asystole at the time of cardiac arrest.

**Conclusions:** Patients who are critically ill, with several co-morbid factors, the likely hood of having SCD is very high. In hospital patients who are at high risk of SCD, placing an AED could reduce the incidence of sudden death by about 30–35%. Further prospective studies should be done in hospitals, because 97% were diabetics Type II and 3% Type I. The prevalence of D in PR. is 12% vs. 8% in the U.S.A. The lipid profile was normal with a cholesterol= 166 ± 25mg%, HDL= 48 ± 8mg%, LDL= 85 ± 16mg%, triglycerides 60 ± 6mg%. The genetics of the puertorrican population is more influenced by Spanish and Indian cultures. Probably, this will produce a less aggressive disease. Less aggressive is defined as less ventricular tachycardia, myocardial infarction and strokes.

**Conclusions:** These findings suggest that genetics and culture is an important aspect in the clinical manifestation of Mets.

**P4** HIGH CUMULATIVE RADIATION DOSE OF PATIENTS UNDERGOING NUCLEAR MYOCARDIAL PERFUSION IMAGING

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**Purpose of Study:** The single medical diagnostic test with the highest radiation burden is myocardial perfusion imaging (MPI), which accounts for >10% of all radiation exposure to the U.S. population. Many patients undergoing MPI receive repeat tests or additional procedures exposing them to ionizing radiation, but no data are available on the total radiation burden.
The purpose of this study is to characterize cumulative radiation doses and repeat testing of patients undergoing MPI.

Methods Used: This retrospective cohort study included 1097 consecutive patients undergoing index MPI. Two electronic health records systems were searched to identify all procedures performed before and after the index procedure. Effective dose of radiation from each procedure was estimated, based upon patient-specific information (e.g. administered activities of radiopharmaceuticals, kerma-air product) and standard conversion factors when available, else upon standard values for the type of study.

Summary of Results: Patients receiving index MPI underwent a mean of 23.9 procedures involving ionizing radiation; a mean of 6.5 were high-dose procedures (>3 mSv, the average annual background radiation in the US). These included a mean of 1.8 MPI studies per patient. 39% of patients had repeat MPI exams, including 5% of patients with ≥5 MPI exams. Mean cumulative dose from MPI alone was 44.6 mSv (median 28.9 mSv, range 6.5–407 mSv). The mean cumulative effective dose for all medical testing was 96.5 mSv, approximately equal to the maximal allowable radiation dose to nuclear industry workers over a 5-year period (median 64.0 mSv, range 6.5–918 mSv). 6% of patients received cumulative doses >100 mSv from MPI alone. 31% of patients received a cumulative effective dose for all medical sources of >100 mSv, including 11% of patients with cumulative dose >200 mSv.

Conclusions: Patients undergoing MPI typically receive many tests involving exposure to ionizing radiation and high cumulative dose. Repeat MPI testing is common. The benefits of medical imaging need to be weighed against radiation-associated risks. Development and validation of strategies that reduce the cumulative amount of radiation patients receive from medical testing, while ensuring that therapeutic decisions remain based on adequate diagnostic information, is essential.

P5 G-GLYCOPROTEIN DOES NOT CONTRIBUTE TO GLUCOCORTICOID EFFLUX IN A RESPIRATORY EPITHELIAL CELL MODEL

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Purpose of Study: Several mechanisms of glucocorticoid (GC) resistance in asthma have been identified, including GC-resistant genes and defective GC receptor binding and nuclear translocation. P-glycoprotein (P-gp), a ubiquitous ATP-dependent efflux transport protein expressed on airway epithelium, is known to transport GCs. High levels of P-gp expression have been found in patients with other GC-resistant inflammatory conditions, such as inflammatory bowel disease, lupus, and rheumatoid arthritis, suggesting that the role of P-gp as a steroid transporter contributes to GC resistance. To investigate whether P-gp can contribute to GC resistance in asthma by testing whether decreasing P-gp expression in dexamethasone (DEX)-exposed respiratory epithelial cells in vitro results in higher intracellular DEX levels.

Methods Used: We transfected A549 respiratory epithelial cells with small interfering (si)RNA targeted at mRNA for MDR1, the gene encoding P-gp. Transfected cells were exposed to 100nM fluorescently-labeled DEX for 15 minutes. siRNA transfection efficiency, surface P-gp, and intracellular DEX were measured by flow cytometry.

Summary of Results: MDR1 siRNA transfection decreased P-gp expression by 20% when compared to nonsense siRNA transfection (geometric mean±SEM nonsense vs. MDR1=389±64 vs. 311±13). This decrease in P-gp expression resulted in decreased intracellular DEX. Specifically, transfected cells that were P-gp- were 3 times less likely to be DEX+ than P-gp+ cells (mean±SEM: 7.2± 19.4% of transfected cells; P = 0.02).

Conclusions: These results are contrary to our hypothesis that decreasing P-gp expression in respiratory epithelial cells decreases cellular efflux of DEX. In fact, our results show a positive relationship between P-gp expression and intracellular DEX. There is some evidence that expression of P-gp may actually be enhanced by GCs. Therefore, our data do not support the concept that P-gp contributes to GC efflux in respiratory epithelium.

P6 NEWBORNS IN THE EMERGENCY DEPARTMENT: WHAT’S THE HARM?

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Purpose of Study: Newborns comprise over 2500 visits to our Emergency Department (ED) annually. Parents who are unable to identify a medical home early in a child’s life may have poorly developed parenting skills and a lack of psychosocial resources. We hypothesized that an ED visit by an infant in the first thirty days of life (newborn visit) for a non-emergent complaint is associated with a high rate of subsequent ED visits and an increased risk of child abuse and/or placement in foster care.

Methods Used: A retrospective cohort study compared 165 newborns presenting for emergent visits with 163 newborns presenting for non-emergent visits. We compared rates of ED visits over the subsequent 2 years. In the second part of our study, a case-control series compared rate of newborn visits among 703 foster children, 703 children with physical or sexual abuse, and 703 controls.

Summary of Results: In the retrospective cohort study, infants with non-emergent newborn visits had an average of 4.52 (SE0.27) ED visits over the subsequent two years compared to infants with emergent visits had 2.5 (SE0.17) subsequent visits (difference = 2.02[95%CI = 2.73 to 1.49]; P < .001). Our case-control series found that abused children were less likely to have had a newborn ED visit than controls (OR = 0.54[0.37-0.77]). There was no association between foster care and newborn ED visits when compared to controls.

Conclusions: Non-emergent ED visits in the first 30 days of life are associated with increased rates of subsequent ED use. Contrary to our hypothesis, abused children are less likely to have presented to the ED in the first 30 days of life. This may indicate that presenting to the ED for a non-emergent reason in the newborn period shows increased parental concern, which may be a factor in decreasing the rates of future child abuse. There was no association between foster care placement and newborn ED visits. Given that many families use the ED in the newborn period for non-emergent care, we envision development of a teachable moment for all newborn discharges to provide guidance for the new parents and to confirm a follow-up appointment with a primary care provider.

P7 RELATIONSHIP BETWEEN FRAMINGHAM RISK SCORE AND METABOLIC SYNDROME FOR PREDICTING CORONARY ARTERY DISEASE


Purpose of Study: The Framingham Risk Score estimates patients’ risk of cardiovascular events. The metabolic syndrome (MetS) has been shown to increase patients’ risk of cardiovascular events. The purpose of this study was to examine how the presence of metabolic syndrome influences the presence of obstructive coronary artery disease (CAD) at different Framingham risk levels.

Methods Used: This study included 1000 patients with no history of CAD who presented for elective cardiac catheterization. The study group had a mean age of 62.6 ± 11 years, and was comprised of 571 men and 429 women. Patients were evaluated for MetS using the NCEP-ATP III criteria. Framingham risk groups were divided into tertiles (0–10%; 11–20%; >20% risk). Significant CAD was defined as the presence of at least 70% in a major coronary vessel and/or 50% stenosis in the left main coronary artery.

Summary of Results: CAD was present in 451 patients, and MetS was present in 486 patients. Patients with MetS were significantly more likely to have CAD than patients without MetS (51.4% vs 43%, p<0.01). Increasing Framingham risk tertiles were significantly more likely to have CAD (35.5% vs 58.4% vs 71.6%, p<0.01 for each comparison). Results from evaluating the effect of MetS on CAD at different tertiles of Framingham risk are revealed in the table below.
Multivariate analysis showed that the Framingham Score is a significant predictor of CAD; the addition of MetS does not add to CAD prediction, and there is no significant interaction noted.

**Conclusions:** Assessing MetS does not affect the incidence of obstructive CAD at any Framingham Risk level.

<table>
<thead>
<tr>
<th>Framingham Risk 0-10%</th>
<th>CAD+</th>
<th>CAD-</th>
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<tbody>
<tr>
<td><strong>MetS+</strong></td>
<td>92</td>
<td>157</td>
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<table>
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<tr>
<th>Framingham Risk 11-20%</th>
<th>CAD+</th>
<th>CAD-</th>
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</thead>
<tbody>
<tr>
<td><strong>MetS+</strong></td>
<td>79</td>
<td>46</td>
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<table>
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<tr>
<th>Framingham Risk &gt; 20%</th>
<th>CAD+</th>
<th>CAD-</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MetS+</strong></td>
<td>68</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>38</td>
<td>20</td>
</tr>
</tbody>
</table>

**P8**

**PEDIATRIC RESIDENT KNOWLEDGE AND COMFORT LEVEL WITH RESUSCITATION FOLLOWING AN EDUCATIONAL INTERVENTION**

M. Lorch, D. Agrawal, K. O’Connell Emergency Medicine, Children’s National Medical Center, Washington, DC.

**Purpose of Study:** To determine if rising second year residents’ comfort and knowledge levels with resuscitation protocols and procedures are improved following an educational intervention.

**Methods Used:** Rising second year general pediatric residents at an urban pediatric teaching hospital were exposed to an eight hour educational session consisting of didactic lectures, stations and mock codes using high fidelity simulation. Residents were asked to complete a survey before and after the intervention describing their experience and comfort level with performing or teaching resuscitations and procedures, as well as answer content based questions to assess their knowledge of resuscitative interventions.

**Summary of Results:** Of 24 residents surveyed, 2 had led a code, 5 had obtained central venous access, 1 had inserted an intraosseous (IO) needle, and 6 had performed endotracheal intubation. For questions surrounding comfort with procedures, including calling and leading a code, obtaining intravenous (IV) or IO access, and airway management, 16 of 18 questions showed a significant change (p<0.05) in mean score from pre to post survey responses. The mean increase in comfort level for performing procedures ranged from 0.2–1.8 on a 5 point Likert scale and the mean increase in comfort level for teaching a procedure ranged from 0.2–2. The questions with the greatest mean difference concerned teaching peripheral IV and IO needle insertion (p<0.001). The mean difference between pre- and post-intervention content based question scores was 23.9% (95% CI 14–34) (p<0.001).

**Conclusions:** During their first year of training, pediatric residents had little experience and felt uncomfortable with resuscitative interventions. An educational review improved their knowledge and comfort level with these skills. As they graduate to become senior residents, a hands-on review of procedures and practice using mock code simulations provides residents with not only the knowledge and skills to provide better care to patients, but also instills the confidence needed to teach these skills to others.

**P9**

**PATHOLOGY OF SOME OBSTETRIC-PEDIATRIC INTERVENTIONS**

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**Purpose of Study:** Many perinatal-pediatric interventions are thought to be safe but the pathology and effects on lab data are poorly known. Labor manipulation by forceps or vacuum assist devices (VAD) has risks. Moribund infants are often revived by intraosseous tibial injection (ITI) to force fluids into the circulation.

**Methods Used:** Five cases: 2 VAD, 2 ITI, and 1-both. One, by section after 4 failed VAD, survived; the placenta revealed trauma. The others were autopsied.

**Summary of Results:** Male, 3370 g, born vaginally post 4 failed VAD, died at 136 hrs with marked angulation of medulla and upper spinal cord, cerebellar tonsil herniation, and prokörper necrosis. #2: 16 day male, 3200 g, vaginal birth after 3 VAD; infant collapsed at home; no evidence of overlay, suffocation, or external trauma. Posterior skull had subclinical incomplete fracture lines subtended by small old subdural hemorrhages, thickened dura, and hemosiderosis. Attempted ITI resulted in fat emboli to lung, a brief but not sustained heart response. #3: section delivery after 4 failed VAD and lacerated lower uterine segment, 3+ bleeding after 4th VAD; 3500 g male had skull fracture but survived with massive hemispheric infarction, left middle cerebral artery field. Laceration of surface placentas vessels and numerous intraplacental air emboli were identified. #4: 7.5 month female with incomplete immunsizations died in a pertussis epidemic with bronchiolitis, pneumonia, and severe acute meningitis. Forceful left ITI dislocated the superior epiphyseal plate, releasing multiple fat emboli to lung. #5: 28 month female with multiple traumatic injuries resuscitated by 3 ITI before admission; 10 minutes later many myelocytes and bands were in the WBC; serum lipase was 1100 U/dl; at 16 hrs no myelocytes were seen; lipase was normal. Autopsy after 44 hr survival found many fat emboli in lung and more recent fat emboli in brain, adrenal capsule, kidney.

**Conclusions:** VAD may cause significant fetal and placental trauma. The number of tries and results should be included in the clinical summary and those placenta examined thoroughly. Emergent ITI causes marrow and fat emboli with potential to worsen the clinical status of the child. Recipient tibias should be studied pathologically for disruption, hemorrhage, and trauma to the epiphysial plate, and brain and lung tissue frozen for fat stain.

**P10**

**LONG-TERM EFFECTS OF A MOCK CODE CURRICULUM ON PEDIATRIC RESIDENT EDUCATION**

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**Purpose of Study:** To assess the impact of a three year mock code curriculum on pediatric residents’ 1) attendance at actual and mock codes, 2) anxiety level, capability in running and comfort with knowledge in codes, and 3) taking an active or leadership role in codes.

**Methods Used:** Pediatric residents at a large, urban tertiary care children’s hospital were anonymously surveyed about their experiences in and self-perceptions regarding codes before initiating a monthly mock code curriculum (Year 0) and three years after its onset (Year 3). Residents rated the curriculum’s effectiveness in improving their education and participation in codes. A Likert Scale was used to report: anxiety level and capability in running codes, changes in comfort with code knowledge, and participation in actual codes due to the curriculum. Responses from Years 0 and 3 were compared.

**Summary of Results:** 61 (66%) residents in Year 0 and 76 (92%) in Year 3 completed the survey. Residents in Year 3 observed and participated in more mock codes (p<0.001), but not in more actual resuscitations (p=0.209). Year 3 residents had lower odds of feeling anxious in a code and higher odds of feeling capable of running a code and comfortable with code knowledge. There was no difference in active or leadership roles (see Table). 96% of residents felt that the curriculum increased their comfort and knowledge in codes, 78% felt that mock codes increased their participation in actual codes, and 99% felt the curriculum was useful in overall residency training.

**Conclusions:** A three year mock code curriculum helps residents feel more comfortable with knowledge, less anxious, and more capable of running a code. The curriculum increased residents’ participation in mock codes. Residents believed the curriculum was a useful part of their training.

<table>
<thead>
<tr>
<th>Resident Perspectives</th>
<th>Odd Ratio (Year vs. 0)</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>Anxiety in a resuscitation</td>
<td>0.33</td>
<td>0.16-0.70</td>
</tr>
<tr>
<td>Capability in running a code</td>
<td>6.3</td>
<td>2.8-14.2</td>
</tr>
<tr>
<td>Comfort with code knowledge</td>
<td>4.3</td>
<td>2.1-8.9</td>
</tr>
<tr>
<td>Active role in ≥1 code</td>
<td>0.89</td>
<td>0.34-2.1</td>
</tr>
<tr>
<td>Leader in ≥1 code</td>
<td>0.86</td>
<td>0.34-2.2</td>
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</tbody>
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P11
CARDIAC MRI ANALYSIS OF RIGHT VENTRICULAR FUNCTION IN VALVULAR HEART DISEASE
A. Nasur1,2, R. Chintala1, M. Greenberg1,2, G. Trachiotis2 2Cardiology, Howard University Hospital, Washington, DC 2VA Medical Center, Washington, DC.

Purpose of Study: In valvular heart disease, elevated left atrial and pulmonary artery pressures (PAP) can lead to right ventricular strain and right ventricular failure. Elevated left ventricular end-diastolic pressure (LVEDP) and PAP are risk factors that influence survival after valve surgery. Accurate quantification of right ventricular function can be assessed by cardiac MRI (cMRI). The relationship between cMRI analysis of RVEF and cardiac hemodynamics with regard to outcome remains undefined.

Methods Used: Between January 2004 and February 2008, 49 consecutive patients undergoing valvular heart surgery (40 AVR, 6 MVR, 3 TVR) had preoperative cardiac catheterization and cMRI. 93% were males, average age = 65 yrs (39–83), and a majority of patients had diabetes, and hypertension. Cardiac MRI was performed by one technician and all studies analyzed by one cardiologist. Preoperative PAP and LVEDP were compared to RV cMRI analysis to determine (1) relation of RVEF to severity of pressure overload on the right ventricle and 2prognostic value of RVEF in patients undergoing valvular heart surgery.

Summary of Results: By cardiac catheterization, LVEDP was 23.3 ± 13 mmHg and PAP was 41 ± 14 mmHg, signifying significant elevated left and right sided pressures. By cMRI, LVEF was 57 ± 16% and RVEF was 47.8 ± 10%, both in near normal range; however, RVEDV was 103.5 ± 80 mm, which represents mild RV volume overload. For the group, risk adjusted estimated mortality was 6 ± 5%(1.2–5.5%); yet actual mortality was only 4% (n = 2).

Conclusions: In patients presenting for valvular heart surgery, accurate LV and RV function and morphology can be assessed by cMRI. Despite significantly elevated left and right-sided pressures, preservation of RVEF is generally maintained, and likely serves as a better predictor of outcome than hemodynamics after valvular heart surgery. For patients with preoperative data suggesting RV dysfunction, accurate RVEF by cMRI can give added morphologic and prognostic information.

P12
EPIDEMIOLOGY OF PEDIATRIC FOREARM FRACTURES IN WASHINGTON DC, 2003–2006

Purpose of Study: Forearm fractures account for 25% of all fractures in children. These fractures result in substantial morbidity and estimated costs exceeding $2 billion dollars per year in the United States. Despite the success of public health efforts in the prevention of other injuries, the incidence of pediatric forearm fractures is increasing for unclear reasons. The epidemiology of these injuries, including mechanism of injury, has not been well described in the pediatric population. Our objective was to characterize the epidemiology of forearm fractures in children evaluated in an urban pediatric emergency department (ED).

Methods Used: This retrospective study included Washington DC children, ages 0–17, treated for an isolated forearm fracture in the Children’s National Medical Center ED from 2003–2006. Patients with bone mineralization disorders and repeat ED visits for the same fracture event were excluded. Chart review was done to obtain demographic and clinical data. Descriptive epidemiologic and bivariate analyses were conducted.

Summary of Results: This preliminary analysis included 929 patients. The majority of patients were male (64%) and African-American (80%). The mean age (± SD) was 8.4 years (± 3.9). Weight-for-age percentile was greater than or equal to 95% in 24.1% of cases. Most forearm fractures occurred during the spring season. The most common mechanism of injury was fall-related (83%) whereas direct trauma caused 10% of fractures. Fall from monkey bars was the specific mechanism in 17% of all cases. Of the 593 cases in which a detailed mechanism was described, 539 fractures (91%) resulted from minor trauma. The mechanism of injury in 42% of minor trauma-related forearm fractures was a fall from standing height.

Conclusions: Falls from monkey bars and minor trauma are implicated in the majority of childhood forearm fractures. Prevention strategies should target playground safety. Further research is needed to evaluate factors, including obesity and bone health, which may contribute to forearm fracture risk associated with minor trauma.

P13
PATIENT CHARACTERISTICS ARE ASSOCIATED WITH ED OUTCOMES FOR CHILDREN
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Purpose of Study: The study’s objective was to describe the patient characteristics associated with ED outcomes for children.

Methods Used: Data were obtained from AHRQ’s 2007 NJ State Emergency Department Database. Patient characteristics including age, race, payer and diagnosis were investigated and compared across the outcomes of mortality, left without being seen (LWBS), and length of stay (LOS). Bivariable analyses compared outcomes with patient characteristics using the Chi square test. Analyses were performed using SPSS (Version 17.0); p-values < 0.05 were significant.

Summary of Results: Age, race and insurance status were associated with ED outcomes. A biphasic relationship was noted for age and ROS; youngest and oldest patients had ED LOS > 6 hours (OR 1.2, p-value < .001) and a high odds of LWBS (OR 1.5; p-value <.002 for infants < 1 month and OR 1.3; p-value <.001 for infants < 12 months). White patients had the lowest ED mortality (0.02%), LWBS rate (0.51%) and LOS (4.0 hours). Minority patients had the highest mortality (OR 2.6 for Blacks; p-value <.001) and a high odds of LWBS (OR 1.6; p-value <.001 for Blacks and OR 1.8; p-value <.001 for Hispanics). Privately insured patients had the lowest mortality (0.02%) and odds of LWBS (OR 1.3; p-value <.001) compared to self pay patients (OR 4.9; p-value <.001 and 2.2; p-value <.001, respectively) or Medicaid (OR 1.5; p-value 0.032 and 1.8; p-value <.001, respectively). Children with chronic conditions (CC) had an ED visit rate of 7.1% with the most frequent CCs being respiratory (3.2%) and mental CCs (2.4%). Patients with CCs were more likely to die (OR 26.1; p-value <.001) and to have ED LOS > 6 hours (OR 2.0; p-value <.001) than those without CCs.

Conclusions: Patient characteristics including age, race, insurance status and diagnosis demonstrated important associations with outcomes of ED care.

P14
HEMOLYTIC AND THROMBOGENIC CHARACTERISTICS OF ECMO SYSTEMS AT SIMULATED FLOW RATE FOR NEONATES
A.D. Meyer, A.A. Wiles, O. Rivera, E.C. Wong, R.J. Freishtat, K. Rais-Bahrami, H.J. Dalton 1Children’s National Medical Center, Washington, DC 2Phoenix Children’s Hospital, Phoenix, AZ.

Purpose of Study: Modern centrifugal pumps/hollow-fiber oxygenator systems for extracorporeal membrane oxygenation (ECMO) have advantages such as less priming volume, ability to place the pump at any level in relation to the patient, and no pressure generation that can lead to tubing rupture as compared to the more commonly used roller-head/silicone membrane systems. Adoption of the centrifugal pump/hollow fiber oxygenator system has been slow due to past evidence of severe hemolysis leading to subsequent renal failure and mortality. Another complication of the neonate on ECMO is intracranial hemorrhage, which can be caused by platelet dysfunction. Little data exists comparing the modern centrifugal pump/hollow-fiber oxygenator system vs. roller-head/silicone membrane system for their hemolytic and platelet function at low flow rates consistent with neonatal ECMO. The purpose of this research is to choose a system that is optimal for neonatal care.

Methods Used: In a pilot analysis, two newer components (Jostra Rotaflow pump and Quadrox-D oxygenator, Maquet, Wayne, NJ) were compared to the standard roller-head pump (Jostra, Maquet, Wayne, NJ) and silicone membrane oxygenator (Medtronic, Minneapolis, MN) in a simulated in vitro ECMO circuit circulating whole swine blood at 300 ml/min. Four circuit
combinations were examined for hemolysis and platelet aggregation during 6 hrs of continuous use. Hemolysis was measured by plasma free hemoglobin (fPH) using a spectrophotometer. Platelet aggregation was measured using flow cytometry.

Summary of Results: All of the ECMO systems created fPH at a similar rate as compared to the static. There was no difference in the mean fPH for the centrifugal/hollow-fiber oxygenator and the roller/silicone systems, 0.0024±0.0007 (g/100L) versus 0.0024±0.0018 (g/100L), respectively. Preliminary results may show that ECMO systems with a hollow-fiber oxygenator have greater platelet aggregation compared to systems with a silicone membrane oxygenator.

Conclusions: In a low-flow environment, centrifugal/hollow-fiber and roller-head/silicone membrane systems have similar mean index of hemolysis. Further study to confirm these preliminary results and correlate to patient care is warranted.

Methods Used: As an initial test of this hypothesis, HOCl was reacted with dopamine and the products analyzed by spectrophotometry. The chlorination of dopamine resulted in immediate increases in the absorbance at the amine (~205–230 nm) and phenol (~280 nm) regions, as well as, the formation of new product at 460 nm. Addition of HOCl scavengers, including hydrogen sulfide and taurine, blocked the chlorination of dopamine. The content of these scavengers in brain decreases with age and suggests another mechanism by which chlorodopamine formation might be accentuated in Alzheimer Disease. The early reaction products of dopamine and HOCl were also toxic to cultured SH SY5Y cells.

Conclusions: Taken together these observations suggest that the HOCl formed during Alzheimer Disease may chlorinate dopamine and contribute to the parkinsonism exhibited by a portion of these patients.

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Conclusions: Taken together these observations suggest that the HOCl formed during Alzheimer Disease may chlorinate dopamine and contribute to the parkinsonism exhibited by a portion of these patients.
P19
MACROLIDE REPRESSION OF MUC5AC GENE EXPRESSION IN HUMAN LUNG EPITHELIAL CELLS

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Purpose of Study: Overproduction of mucin glycoproteins (mucins) is a characteristic phenotype of chronic lung diseases. Inflammatory mediators upregulate mucin gene expression in vitro while glucocorticoids and macrolides repress mucin gene expression. Macrolide antibiotics have anti-microbial effects but also appear to have an anti-inflammatory role in chronic lung diseases. Whether their reported effect on mucin gene expression in lung epithelial cells is due to a direct effect on gene regulation or through an indirect effect on inflammatory mediators is unresolved. The purpose of this study is to evaluate the effects of two macrolides, azithromycin and erythromycin, on MUC5AC gene expression in lung epithelial cells in a concentration and time based manner and to determine whether macrolides, like glucocorticoids, transcriptionally repress MUC5AC gene expression.

Methods Used: Normal primary human bronchial epithelial (HBE) cells were cultured, differentiated under air-liquid interface conditions, and exposed in duplicate to azithromycin and erythromycin in concentration ranges from 10^-6 to 10^-3 M for 24 h. HBE cells were also exposed to 10^-3 M macrolides for 1, 4, 8, and 24 h. MUC5AC mRNA levels were analyzed by real-time RT-PCR and normalized to β-actin. Transcriptional analysis of MUC5AC gene expression will be performed following transfection of MUC5AC promoter luciferase constructs into lung epithelial cells.

Summary of Results: MUC5AC mRNA levels had a decreasing trend with exposure to erythromycin at concentrations of 10^-6 and 10^-5 M (36% and 45% decrease, respectively) at 24 h. In contrast, MUC5AC mRNA levels decreased 24% at a concentration of 10^-5 M of azithromycin. Experiments to determine the temporal effects of macrolides on MUC5AC gene repression are underway.

Conclusions: Erythromycin exhibited a more potent inhibition of MUC5AC gene expression than azithromycin in primary differentiated HBE cells in the absence of inflammatory mediators, indicating that macrolides, like glucocorticoids, directly repress MUC5AC gene expression. Future experiments will investigate mechanisms whereby macrolides regulate mucin gene expression.
(cytochrome P450 vitamin D 25-hydroxylase). After adjusting for age, gender, and BMI percentile, SNPs were analyzed for associations with the diagnosis of asthma. Within the asthma cohort, SNPs were analyzed for associations with quantitative measures of asthma phenotype traits including spirometry, blood eosinophils (%), and asthma severity scores.

**Summary of Results:** Only the AA genotype for CYP2R1 SNP rs10766197 was associated with the diagnosis of asthma (P=0.044). In the asthma cohort, multiple SNP associations were identified with quantitative asthma phenotype traits. For example, CYP24A1 SNP rs2248137 was associated with lower vitamin D levels (P = 0.006) and a decreased bronchodilator response based on change in FEV1/FVC (P = 0.007). Additionally, VDR SNP rs2228570 was associated with the presence of >1 positive aeroallergen skin test (P = 0.005), increased serum IgE levels (P=0.001), higher nighttime morbidity scores (P = 0.04), and lower baseline spirometric measures (P=0.05).

**Conclusions:** This is the first study demonstrating that variants in genes involved with Hemochromatosis has also been associated with an increased risk of hepatocellular carcinoma (HCC) especially when iron overload and cirrhosis are present. We report a patient with well controlled hemochromatosis developing HCC in the absence of cirrhosis, iron overload and viral hepatitis but with a history of exposure to atomic bomb radiation.

**Methods Used:** Case: A 70 year old Caucasian man with a 35 year history of hemochromatosis presented to his MD for his regular phlebotomy complaining of right upper quadrant discomfort for one month. An ultrasound showed a liver mass. A CT-guided biopsy showed an adenocarcinoma of liver and the patient was referred to our center for further care. Additional history included hypothyroidism, hypertension, gout and hypercholesterolemia. His hemochromatosis was well controlled with frequent phlebotomies and ferritin monitoring, never requiring iron chelation. He denied smoking and alcohol use. As a soldier in the 1950s he was assigned to observe an atomic bomb explosion in the Johnson Islands without protection against radiation.

**Physical Examination:** No stigmata of liver disease. Mild tenderness in the right upper quadrant. No splenomegaly.

**Laboratory:** alpha-fetoprotein: 46.2ng/ml, HBV viral DNA negative, hemoglobin 14.5 g/dl, Iron 31mcg/dl. Total iron binding capacity 193mcg/dl, Percent saturation 16%, ferritin 247.6mcg/l, homozygous for C282Y hemochromatosis gene, AST 305u/l, ALT 312u/l, ALP 34u/l and total bilirubin 0.6. CT of thorax abdomen and pelvis showed no metastasis.

**Histopathology:** On gross inspection liver looked normal with no nodularity. Microscopy showed differentiated adenocarcinoma with non-extensive portal fibrosis without iron deposition.

**Summary of Results:** Death from Hemochromatosis is 219 times likely due to HCC. However occurrence of HCC in the absence of cirrhosis is very rare. Our case represents the fifth reported case of HCC developing in hemochromatosis in the absence of cirrhosis and iron overload in the English literature.

**Conclusions:** We feel that clinicians following such patients should have a low threshold for ordering ultrasound on onset of symptoms or clinical deterioration of liver function.