

Southern Regional Meeting Abstracts

Cardiovascular Club I

11:00 AM

Thursday, February 25, 2010

1 BETA-BLOCKING DRUG USE IN COCAINE ABUSERS: IS IT SAFE AND EFFECTIVE THERAPY IN HOSPITALIZED PATIENTS?

GD. Everett¹, N. Uddin², A. Java³, A. Klotchko³, A. Velazquez³, S. Singapur³, A. Prevost³, R. Rostorfer³, E. Benzaquen³, K. Patel³, V. Patel³, P. Fotso³, L. Ramos³ ¹Florida Hospital Medical Center, Orlando, FL; ²University of Central Florida, Orlando, FL and ³Orlando Health, Orlando, FL.

Purpose of Study: Case reports have suggested that beta-blockers may unpredictably exacerbate hypertension and tachycardia in concurrent cocaine abusers. Physicians avoid beta-blockers in these patients despite the chest pain and hypertension that cocaine may cause. This study was designed to assess the physiological effect of beta-blockers given to cocaine abusers during emergency room and hospital stays when their symptoms warranted beta-blockers but before their use of cocaine was discovered.

Methods Used: A cohort consisting of every patient admitted to a large, urban hospital during a single calendar year, whose urine contained cocaine metabolites, was created. Subjects were included if they had blood pressure and heart rate measurements recorded before and after beta-blockers or other medications were given. 114 subjects met the criteria. Multivariate regression analysis was used to assess the independent effect of beta-blockers on the blood pressure and heart rate. The regression analysis controlled for the effect of each vasoactive medication given to the subjects.

Summary of Results: The subjects were 33% female, 64% black, 27% white and 9% other race. The median age was 43 (23–74). Chest pain (30%) was the most common admission complaint. 5% of subjects had a troponin level of more than 1.0. 14% and 4% of subjects had creatinine values that exceeded 3.0 and 9.0 respectively. The table displays the results of the main analysis: unadjusted and multivariate adjusted effects of beta-blockers on systolic BP, diastolic BP, and heart rate.

Conclusions: There was no evidence of a deleterious or paradoxical effect of beta blockers when administered to patients documented to be using cocaine.

	Unadjusted, Pre-BB	Unadjusted, Post-BB	Unadjusted, Difference	Adjusted, difference
Systolic BP	147.2(26.2)	134.1(20.3)	-13.1*	-6.8*
Diastolic BP	85.1(17.0)	78.9(13.8)	-6.2*	-7.2*
Heart Rate	90.2(26.1)	79.1(13.4)	-11.1*	-1.4

*p<0.01

2 THE EFFECT OF STENOSIS LENGTH AND DIAMETER ON FRACTIONAL FLOW RESERVE IN CORONARY ARTERY DISEASE

B. Mohandas, M. Agrawal, F. Gobal, S. Singla, JK. Bissett, JL. Mehta, R. Sachdeva *UAMS, Little Rock, AR.*

Purpose of Study: Fractional flow reserve (FFR) is currently the gold standard to determine hemodynamic significance of intermediate coronary stenosis. The aim of the study was to examine the effect of stenosis length (LL) and percentage diameter stenosis (%DS) on fractional flow reserve (FFR).

Methods Used: We studied 209 single coronary stenosis in which FFR was performed. Patients with multiple coronary stenosis in the same coronary artery, bypass grafts, bifurcation stenosis and complex calcified stenosis were

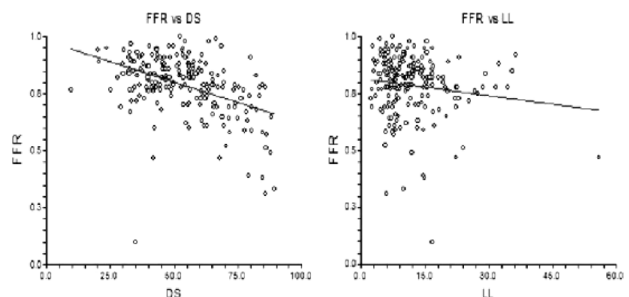
excluded from the study. Peak hyperemia was obtained with either intra-coronary or intravenous adenosine. Offline quantitative coronary angiography (QCA) was conducted to determine LL and %DS.

Summary of Results: The mean LL was 11.64593 ± 7.15985 , mean %DS was 53.7 ± 16.10963 , mean FFR was 0.79 ± 0.12 . We found an inverse correlation of FFR with LL ($r = -0.137$, $p = 0.0469$) and %DS ($r = -0.439$, $p < 0.0001$). In a multiple regression model with both %DS and LL, the association between FFR and LL was non-significant ($p = 0.2206$); and %DS was significant ($p < 0.0001$). Subgroup analysis was performed on stenosis with hemodynamically significant FFR < 0.8 ($N = 101$). Other subgroups analysed were %DS grouped as deciles from 30–70% ($N = 168$); and LL grouped as 5–10 mm, 11–15 mm, 15–20 mm and > 20 mm. There was no significant effect of LL on FFR independent of diameter stenosis in any of the above subgroups.

Conclusions: FFR is inversely associated with both LL and %DS. However, when the effect of %DS is controlled, there is no significant effect of lesion length on FFR.

Effect of LL on FFR independent of %DS.

Effect	Estimate	Standard Error	DF	t value	Pr > t
Intercept	0.9925	0.03005	206	33.02	<0.0001
%DS	-0.00349	0.000513	206	-6.81	<0.0001
LL	-0.00142	0.001154	206	-1.23	0.2206



3 DIFFERENTIAL IMPACT OF BLOOD PRESSURE ON LEFT VENTRICULAR GEOMETRY IN BLACK AND WHITE YOUNG ADULTS: THE BOGALUSA HEART STUDY

J. Wang^{1,2}, W. Chen¹, L. Ruan¹, A. Toprak¹, SR. Srinivasan¹, GS. Berenson¹ ¹Tulane University, New Orleans, LA and ²The First Affiliated Hospital, Shanxi Medical University, Taiyuan, China.

Purpose of Study: Left ventricular (LV) hypertrophy is more prevalent in blacks; hypertension and obesity are more common in blacks than in whites and strongly associated with LV hypertrophy. This study assessed the hypothesis that blood pressure (BP) and obesity measures have a differential impact on LV geometry in black and white young adults.

Methods Used: The study cohort consisted of 1123 subjects (780 whites and 343 blacks; 42% males; age = 24–47 years) enrolled in the Bogalusa Heart Study. LV structure was measured by a two-dimensional guided M-mode echocardiography. Normal geometry, concentric remodeling, eccentric and concentric hypertrophy were defined by LV relative wall thickness and LV mass indexed to height (gram/height to power 2.7). The predictive values of BP and body mass index (BMI) were compared by receiver operating characteristic (ROC) curves.

Summary of Results: Blacks versus whites and males versus females showed significantly greater LV mass index. Blacks versus whites had higher prevalence of both eccentric (15.7% vs 9.1%, $p < 0.001$) and concentric hypertrophy (9.3% vs 4.1%, $p < 0.001$). In separate multivariable logistic regression analysis models, adjusting for age, sex, glucose, triglycerides, HDL and LDL cholesterol, BMI was associated with eccentric hypertrophy (odds ratio (OR) = 1.2, $p < 0.001$) and with concentric hypertrophy (OR = 1.1, $p < 0.01$) in both races. Systolic BP was associated with eccentric hypertrophy (OR = 1.2, $p = 0.002$) in blacks only and with concentric hypertrophy in both races (OR = 1.03, $p = 0.042$ in whites; OR = 1.1, $p < 0.001$ in blacks); diastolic BP showed similar trends. Data on the area under the ROC curve, measured by c statistic, showed that systolic BP had a significantly greater predictive value in blacks versus whites for eccentric hypertrophy ($c = 0.601$ vs 0.501 , $p = 0.008$) and concentric hypertrophy ($c = 0.719$ vs 0.594 , $p < 0.001$). However BMI did not show such a race difference in the predictive values.

Conclusions: These findings indicate that BP levels have a differential impact on the LV geometric changes in black and white young adults, suggesting a potential divergence in mechanisms underlying the target organ damage in the black and white populations.

4 MORTALITY PREDICTION BY DIFFERENT INDEXATION METHODS FOR LEFT VENTRICULAR MASS BY OBESITY STATUS IN 47,865 PATIENTS

DA. Patel¹, C.J. Lavie², RV. Milani², HO. Ventura² ¹Ochsner Clinic Foundation, New Orleans, LA and ²Ochsner Clinic Foundation, New Orleans, LA.

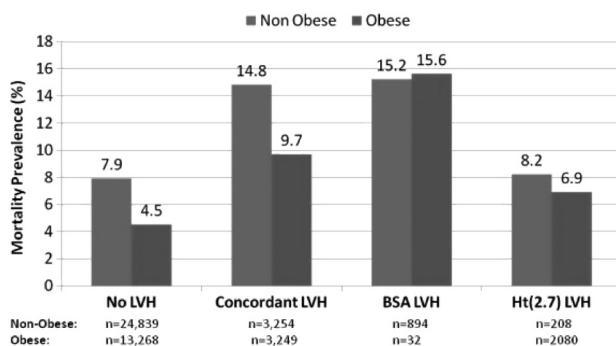
Purpose of Study: Echo-determined LV mass (LVM) is often indexed to body surface area (BSA), but this may not accurately characterize the influence of obesity on LVM and related mortality.

Methods Used: We evaluated 18,630 obese (BMI ≥ 30 ; age: 59 ± 14 yr) as well as 29,235 non-obese (BMI < 30 ; age: 63 ± 17 yr) with preserved EF to determine the impact of LVM indexed to either BSA or Ht2.7 on mortality during mean follow-up of 1.7 ± 1.0 yrs.

Summary of Results: Compared to non-obese, obese had higher LVM index (LVM/BSA: 84 ± 30 vs. 88 ± 27 g/m², $p < 0.0001$; LVM/Ht2.7: 37 ± 13 vs. 45 ± 15 g/m^{2.7}, $p < 0.0001$). Both indices were significantly correlated, albeit less so in obese than non-obese ($r = 0.92$ vs. 0.97). In non-obese patients, LVH determined by LVM/BSA predicted increased mortality compared to patients without LVH (15.2% vs. 7.9%, $p < 0.0001$) whereas LVH determined by LVM/Ht2.7 did not (8.2% vs. 7.9%, $p = \text{NS}$). However, in obese patients, LVH determined by LVM indexed to either BSA (15.6% vs. 4.5%, $p < 0.0001$) or Ht2.7 (6.9% vs. 4.5%, $p < 0.0001$) was associated with higher mortality compared to patients without LVH. Of note, significant difference in mortality was noted in non-obese vs. obese patients with LVH determined by LVM/Ht2.7 (8.2% vs. 6.8%, $p < 0.001$) whereas LVH determined by LVM/BSA failed to demonstrate such difference (15.2 vs. 15.6%, $p = \text{NS}$)(figure).

Conclusions: 1) LVM corrected by either BSA or Ht2.7 predict mortality, both in non-obese and obese patients; 2) differences between the two LVM indexing methods were noted, particularly in patients with obesity.

Mortality associated with echocardiographically determined LVH based on LVM indexed to BSA or Ht^{2.7} by obesity status



Adult Clinical Case Symposium

1:00 PM

Thursday, February 25, 2010

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8 CASES OF RARE DEMYELINATING CENTRAL NERVOUS SYSTEM DISEASE

C. Rincon-Rosenbaum, E. Segura-Palacios, A. Gutierrez *LSUHSC, New Orleans, LA.*

Case Report: Purpose of the Study: Neuromyelitis Optica (NMO) is a rare, life-threatening demyelinating disease involving the central nervous system which affects the optic nerves and spinal cord. NMO was once considered a variant of Multiple Sclerosis (MS) but recent advances have demonstrated unique clinical, laboratory and immunological profiles in NMO. Accordingly, the most common misdiagnosis of NMO is MS. Distinguishing the two diagnoses is critical as the standard and more costly treatments for MS are not effective for NMO. The purpose of this study is to present 8 cases of NMO where treatment was delayed due to misdiagnosis.

Methods of Study: A retrospective review of patients seen in the LSUHSC Neurology clinic from 2002 through 2009 identified 8 cases of NMO, all of which were initially misdiagnosed. The cases are reported with an emphasis on key clinical factors that aid in a differential diagnosis of NMO.

Summary of Results: The 8 cases identified included 6 females and 2 males, aged 12 to 48 years. Six patients had optic neuritis as a clinical manifestation and the average time between initial symptoms and diagnosis was 4.7 years (range: 3–13 years). The most frequent misdiagnoses were MS and neurological manifestation of Lupus. Some patients had received steroid treatments, as well as immunomodulatory agents used in MS. As expected, these prior treatments had been unsuccessful.

Conclusions: NMO can be a devastating, idiopathic demyelinating disease of the central nervous system. Delays in diagnosis can only lead to delays in effective treatment resulting in a measureable economic burden to the patient but an even more important immeasurable cost to long-term health and quality of life. Careful review of the clinical presentation can help with a differential diagnosis; however the most effective tool may be a simple blood test which identifies the highly specific serum antibody marker (NMO-IgG). This blood test should be used routinely in complex clinical presentations where NMO is a possibility. Making a correct diagnosis shortly after symptom presentation should reduce the economic burden of ineffective treatments and repeated evaluations and may greatly improve the long-term outcome in persons with NMO.

6

ARTIFACT ON Tc-99m GATED SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (GSPECT) IMAGING: ECTOPIC KIDNEY MIMICKING AS POSTERIOR WALL OF LEFT VENTRICLE

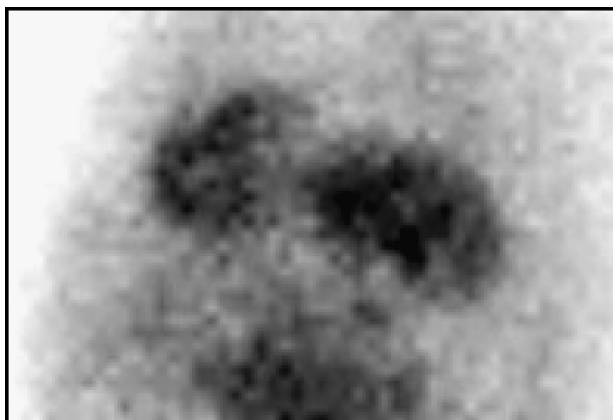
A. Bienek, Y. Yaqub, G. Meyerrose, K. Nugent *Texas Tech University, Lubbock, TX.*

Case Report: Introduction: The Tc-99m GSPECT images are widely used for detection of reversible myocardial ischemia. The uptake of contrast by the gastrointestinal tract is a well known finding and can mimic findings of reversible ischemia.

Case Report: A 63-year-old man with a history of coronary artery disease and hypertension presented with chest discomfort. He underwent a CT of the chest and abdomen and treadmill stress test with Tc-99m GSPECT imaging. These images showed increased contrast activity lateral to myocardium. After reviewing gated images in this patient, it was initially thought that this image represented left ventricular posterior wall (LVPW) or upper gastrointestinal contrast uptake that was interfering with SPECT imaging (Fig 1). Soda water had been given to patient at the beginning of test to decrease GI uptake. This led to the suspicion of LVPW contrast uptake or uptake by an extra intestinal source. A previous CT-scan of thorax and abdomen revealed elevation of left hemi-diaphragm and left kidney, and intra thoracic left kidney uptake was the culprit artifact. The left kidney corresponded to the area of increased uptake seen on the Tc-99m Myoview GSPECT scans, and this resolved the conflict.

Discussion: A thoracic kidney is a rare anomaly and occurs mostly in the form of ectopic kidneys. The literature rarely reports an intra-thoracic kidney detected on GSPECT Tc-99m images masquerading as LVPW and

presenting a diagnostic dilemma. A high index of suspicion should be maintained about the possibility of artifacts on the GSPECT Tc-99m Myoview images which can be an anatomical variation confounding the diagnostic utility of GSPECT imaging.



7

CASE REPORT: WEISSELLA CONFUSA BACTEREMIA IN A LIVER TRANSPLANT PATIENT WITH HEPATIC ARTERY THROMBOSIS

N. Harlan¹, RR. Kempker², EM. Burd³, DT. Kuhar² ¹Emory University, Atlanta, GA; ²Emory University, Atlanta, GA and ³Emory University, Atlanta, GA.

Case Report: A 54 year old man with a history of non-alcoholic steatohepatitis and hepatocellular carcinoma presented two months after an orthotopic liver transplant with fever and abdominal pain. Two weeks prior he had a hepatic artery thrombosis and a biliary stricture for which a hepatic artery stent and a biliary stent were placed. Laboratory workup was significant for leukocyte count of 7800/mcl with 92% segmented neutrophils, hemoglobin 9.4 gm/dl, alanine aminotransferase 98 unit/L, aspartate aminotransferase 72 unit/L, alkaline phosphatase 358 unit/L, albumin 2.8 mg/dl, and total bilirubin 1.6mg/dl. A computed tomography scan of the abdomen and pelvis revealed multiple small fluid collections in the liver consistent with bilomas, and a hepatic angiogram showed complete occlusion of the common hepatic artery stent. Two sets of blood cultures were positive for an organism initially identified by MicroScan as an alpha-hemolytic *Streptococcus* species. However, the identification was in question because the organism was resistant to vancomycin. Two days later, additional tests showing positive hydrolysis of esculin and arginine confirmed the organism as *Weissella confusa*. *Weissella confusa* is a Gram-positive coccobacillus which may be misidentified as *Leuconostoc* when cultured. It is commonly found in sewage, carrots, sugar cane, fermented foods, and intestinal flora. While only 4 cases of clinical infection with *W. confusa* have been described previously, *W. confusa* has been isolated from the stool of liver transplant patients, and may be an underreported cause of infection due to improper identification. As it can cause clinical infection in these immunosuppressed hosts, identification of this organism is paramount because it is often vancomycin resistant, and incorrect identification could lead to improper antimicrobial selection and ultimately worsened patient morbidity or mortality.

8

NEED A LITTLE BIT OF KETCHUP WITH THOSE FRIES?

E. Kauffman, LS. Engel *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: Differentiating delirium and psychosis can be a diagnostic conundrum, particularly if complicated by illicit agents. The deceptive clinical picture can confuse even the most astute physician.

A 28-year-old man with no past medical or psychiatric history presented to the emergency department with his family complaining of fever and "feeling weird"-described as visual and auditory hallucinations, some paranoia, and a mild headache. The patient's family noted that he had been somewhat agitated and violent over the last couple of hours. During his exam,

he was agitated with intermittent outbursts and auditory hallucinations. No focal neurological deficits or meningeal signs were evident. Serum and urine toxicology studies were positive for marijuana (THC). The patient admitted to smoking a "few joints daily" with last use approximately 24–48 hours from admit. Basic labs and head CT were unremarkable. A lumbar puncture was performed with normal opening pressure, normal glucose and protein, 35 white cells with slight lymphocytosis. Gram stain was negative. There was some concern for encephalitis, so spinal fluid was sent to evaluate for herpes virus and arbovirus. The patient was treated with haldol and ativan for his persistent agitation and empiric antibiotics for meningitis. Psychiatry was consulted with thought of new onset psychosis due to schizophrenia with plan for inpatient psychiatric evaluation. However, within 36 hours of admission the patient's symptoms completely resolved. All antipsychotics and antibiotics were discontinued. It was later revealed that the patient had smoked some "fry" or marijuana that is soaked in embalming fluid. The patient was discharged to home on no medicines.

Fry is marijuana or a cigarette that is soaked in embalming fluid (formaldehyde, methanol, ethanol, other solvents and sometimes PCP) then dried. Other names for this drug are Illy, wack, amp, wetdaddy, clickem, and drank. This combination accentuates the hallucinogenic effect of the drug by burning more slowly with effects lasting up to 3–4 days. Smokers can experience paranoia, hallucinations, delusions, memory and speech impairment. Chronic formaldehyde exposure is a carcinogen for head and neck neoplasms. Prolonged hallucinogenic effects of marijuana can mimic new onset psychosis of schizophrenia.

9

RITUXIMAB AS A SUCCESSFUL TREATMENT FOR REFRACTORY UVEITIS IN RHEUMATOID ARTHRITIS

S. Kumar, N. Witty, V. Majithia *University of Mississippi Medical Center, Jackson, MS.*

Case Report: Rheumatoid arthritis (RA) is a complex condition characterized by inflammation in the synovial membranes of joints. Extra-articular manifestations, including uveitis, have been well-described. Rituximab is an anti-CD20 B cell monoclonal antibody used successfully to treat RA. A 50-year-old black gentleman with a long-standing history of seronegative RA was treated initially with prednisone, hydroxychloroquine, methotrexate, and azathioprine. In October 2004, he was referred to ophthalmology for bilateral painful, red eyes. Visual acuity was 20/25 OD and 20/30 OS. Anterior uveitis, also called iritis, was diagnosed by slit lamp examination as was glaucoma with elevated intraocular pressures. Oral steroids were continued while steroid and cyclopentolate eye drops were started. Over the next two years, his RA remained quiet but he had continued flares of iritis requiring adjustments of his eye drops. Due to DMARD intolerance, a TNF-inhibitor was started in July 2007. A month later the patient's illness was complicated by pulmonary *Mycobacterium tuberculosis* (MTB) and *Aspergillus* infections, diagnosed by bronchoalveolar lavage. A year later, after treating both the MTB and fungal infections, the patient was given rituximab 1000mg two weeks apart at six month intervals. Oral steroids and hydroxychloroquine were continued and no side effects were reported. Interval ophthalmologic examinations revealed inactivity of the uveitis but persistence of glaucoma. To date, the patient's RA is stable on rituximab infusions with low-dose prednisone and hydroxychloroquine. His uveitis is also stable off all intraocular therapy. Extra-articular RA manifestations, such as anterior uveitis, pose significant morbidity to the patient by leading to blindness. The immunopathogenesis of RA involves complex interactions between T cells, B cells and macrophages. Traditional treatments for RA including NSAIDs, steroids, and DMARDs as well as biologics are effective. Rituximab, a B-cell targeting therapy, provides an alternative therapeutic intervention in inflammatory conditions. Not only has the rituximab effectively treated our patient's RA, but it also has put the uveitis into remission. Further research is needed to elucidate the benefit of rituximab in the treatment of uveitis.

10

A CASE OF HYPER IgG 4 LUNG DISEASE, A REAL ZEBRA?

S. Meng¹, N. Farah¹, C. Scott-Bennett² ¹University of Mississippi medical, Jackson, MS and ²G.V. (Sonny) Montgomery VA Medical Center, Jackson, MS.

Case Report: Hyper IgG 4 disease is a rare entity that has recently been proposed as a chronic inflammatory process that can involve a variety of organs in different ways. The typical pathology finding is high IgG 4 positive plasma cell infiltrate that lead to dense fibrosis in the involved tissues. Literature has reported multiple conditions relating to high IgG 4 such as retroperitoneal fibrosis, systemic fibrosis, autoimmune pancreatitis, sclerosing cholangitis, orbital pseudotumor, Reidel's thyroiditis, Sjogren's, sclerosing pachymeningitis, etc. So far there is only one case report found in the literature about pulmonary hyper IgG 4 disease. We describe this case to further illustrate that pulmonary hyper IgG 4 diseases does exist. Case report information was obtained through the medical records without identification of the patient information. Literature search was done through Pubmed. Forty two year old African American male with past medical history of optic nerve tumor resection, diverticulosis, hydronephrosis, lung mass, complained of worsening of shortness of breath, low-grade fever, cough, and chest pain. He has a family history of Sjogren's and lupus, and he used to work as a tailor. He is a non-smoker. Multiple evaluations returned as negative including aerobic, anaerobic, AFB fugal, viral, and fungal cultures. EBV, ANA, ESR, CRP, cytology were all negative. He had pulmonary mass on radiology report and had biopsy in 2008 reported as "atypical lymphoplasmacytic infiltrate". SS-A was elevated at 149. He also has mild elevated IgG but normal subclass. Pt had repeat pulmonary biopsy in 2009, and pathology reported as "marked lymphoplasmacytic infiltrates and dense fibrosis, increased number of IgG4 positive cells among the IgG positive plasma cells, highly suggestive hyper IgG 4 lung disease". Oral steroid therapy was started with good response. Patient has sought medical attention for an extended time period without definitive diagnosis. He also has history of an orbital tumor removed many years ago, which could be related to hyper-IgG 4 disease. More knowledge about this syndrome may lead to earlier diagnosis without engagement of extensive investigation, especially since this disease typically has a very good response to steroids.

11 PRIMARY CARDIAC SYNOVIAL SARCOMA - AN EXTREMELY RARE CASE

V. Patel¹, C. Ford¹, D. Bollineni¹, T. Varma², K. Modi¹, MC. Mancini³ ¹LSU Shreveport, Shreveport, LA; ²LSUHSC, Shreveport, LA and ³LSUHSC, Shreveport, LA.

Case Report: Primary synovial sarcomas of the heart comprise less than 0.1% of the cardiac tumors with only two cases reported to originate from left side of the heart. We report a third case.

A 47 y/o white male with only a h/o smoking and family cancer syndrome presented with intermittent shortness of breath and mid-sternal chest pain for one year. Two weeks prior to presentation, he noted new onset cough and rusty sputum with increasing shortness of breath and intermittent palpitations. CXR showed patchy bilateral basilar infiltrates. A CT of the chest and abdomen showed a large soft tissue mass involving the left atrium and ventricle, multiple peripheral lung nodules and mediastinal lymphadenopathy.

A 2D-ECHO followed by TEE with contrast confirmed an extra-cardiac mass posterior to the left atrium with protrusion into the left atrium and through the anterior and posterior leaflets of the mitral valve causing severe diastolic dysfunction. The findings were suggestive of malignancy. Bronchoscopy was negative. Subsequent CT chest revealed regression of the upper lung field infiltrates suggesting more of inflammatory origin. With thorough collaboration of all the services, the decision to operate was made to implement the best treatment for the suspected cardiac malignancy. During surgery, a large globular soft tissue mass measuring 13 X 8.5 X 6.5 cm was resected intact free from the myocardium with a knobby stalk measuring 3 X 5.5 X 2.5 cm originating from the left atrial wall. Histopathology of the tumor revealed a biphasic synovial sarcoma of the heart without epicardial involvement. FISH analysis for SYT/18Q11 was abnormal.

Synovial sarcomas of the heart are extremely rare aggressive tumors and have a poor prognosis with most patients dying within the first year. Recurrences after resection and even with chemotherapy and heart transplant are very likely. Wide surgical resection is the cornerstone of therapy with aggressive follow-up.

Our case is the third reported case of primary synovial sarcoma of the heart originating from the left atrium with positive FISH analysis of characteristic t(X; 18) translocation and is believed to be the largest synovial tumor of the heart reported so far.

12 ACUTE DOPAMINE DEPLETION SYNDROME

E. Singhatiraj, S. Ngamreunphong, K. Nugent *TTUHSC, Lubbock, TX.*

Case Report: Purpose of Study: To present information on an under-diagnosed complication from patient with Parkinson's disease.

Methods Used: Case analysis and literature review

Summary of Results: A 78-year-old woman Parkinson's disease, Alzheimer's disease, and hypothyroidism presented with altered mental status, fever and muscle rigidity for two days. Patient ran out of carbidopa, ectapone, levodopa and amantadine eight days before admission. On exam she was febrile, confused and had generalized rigidity. Laboratory demonstrated a WBC of 13,500/L with 81% neutrophils, BUN 28 mg/dl, creatinine 1.6mg/dl, and CK 893 IU/L. A head CT showed significant generalized cortical atrophy and severe small vessel ischemic disease in the periventricular white matter. She was treated with ceftriaxone, vancomycin, and IV hydration; levodopa was resumed per recommendation of neurologist. Twelve hours after starting treatment patient was less confused, less rigid, and able to communicate. Her fever was subsided and her CK declined. The incidence of acute dopamine depletion syndrome is uncertain. Not all patients with Parkinson's disease who discontinue these medications develop this syndrome. Infections, dehydration and hot weather can trigger this condition without withdrawal of the medication. The pathogenesis of the various clinical features of acute dopamine depletion syndrome is not well elucidated. In NMS dopamine receptors are blocked by neuroleptic drugs. In acute dopamine depletion syndrome sudden drug withdrawal reduces dopamine levels in the CNS. Therefore, impairment of dopaminergic transmission should be the explanation of both syndromes. Treatment should be started as soon as possible with the administration of intravenous fluid, external cooling, and administration of anti-Parkinsonian drugs. Other drugs with clinical efficacy include apomorphine, dantrolene, amantadine and pulsed steroids.

Conclusions: We report a case of acute dopamine depletion syndrome which developed abruptly after stopping her medication. Patients usually present 72-108 hours after withdrawal of medication with fever, rigidity, altered mental status, autonomic dysfunction, and elevated CK. High fever is the most frequent clinical sign, followed by worsening of Parkinsonism and altered mental status. Treatment by resuming of anti-Parkinsonian medications should be started as soon as it is diagnosed.

13 GNAWING GABAPENTIN

PR. Lopez¹, S. Leicht¹, RD. Smalligan² ¹East Tennessee State University, Quillen College of Medicine, Johnson City, TN and ²Texas Tech University Health Sciences Center at Amarillo, Amarillo, TX.

Case Report: A 73yo woman with HTN, prolactinoma, hypothyroidism and post-herpetic neuralgia presented with 1 month of crawling sensations over her entire body along with an extensive pruritic rash. She had no history of skin or psychiatric conditions, travel, outdoor exposure or recent hotel stays and denied systemic symptoms. Chronic meds were unchanged except the recent addition of gabapentin for neuralgia. The patient was convinced she had parasites and felt "bugs" crawling into her nose and laying eggs. She had her house fumigated and tried pesticides on her skin without improvement and was referred to a dermatologist. Meds: bromocriptine, lisinopril, thyroxine and gabapentin. Physical exam: normal except for extensive excoriations with surrounding erythema over her entire body. Labs: normal CBC without eosinophilia, normal CMP, and TSH. After organic causes were ruled out, delusions were considered and gabapentin was discontinued as it was the most recent addition. After 2 wks the symptoms had resolved and all excoriations were healing. The diagnosis of delusions of parasitosis was made and the patient accepted the explanation.

Discussion: Internists are confronted by rashes and other skin conditions on a daily basis. Most of these are due to atopic dermatitis, scabies, poison ivy, skin cancers and other common disorders, but occasionally a more rare entity presents itself. Delusions of parasitosis (DP) is a rare psychiatric disorder in which the patient has a fixed, false belief of being infested with parasites. It occurs primarily in white, middle-aged women and has been associated with anti-parkinsonian agents, ciprofloxacin, doxepin and others. Though generally considered safe, gabapentin has known behavioral side effects including mood changes, agitation and cognitive impairment. While parasitic delusions have not been previously reported with gabapentin, the temporal relationship in our case and improvement after cessation suggests gabapentin may have been responsible. This case reminds physicians

that even when the most common adverse reactions of a medication are well known, a high index of suspicion should be maintained when new symptoms appear following the introduction of a medication.

14

JUST ANOTHER DAY IN THE FAST TRACK

E. Kauffman *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: A 55 year old male presented to the fast track complaining of progressive loss of vision and pain in his right eye for three days. He reported working in a local tomato field while a plane sprayed a chemical across the field. He denied headache or face trauma. Physical exam noted 20/25 vision in the left eye with complete loss of vision in the right eye. The orbital rim and extraocular muscles were intact, but the globe appeared enophthalmic. There was moderate subconjunctival hemorrhage, but no hyphema. A clouded cornea limited the fundoscopic exam. The left pupil was reactive with consensual reflex. A call to the local poison control center noted that sulfa-based agents had been sprayed in the region that week—the effects were inconsistent with the patient's presentation. Bedside ocular ultrasound demonstrated an open globe, complete retinal detachment, lens dislocation, and possible foreign body. Ophthalmology was emergently called and subsequently evaluated the patient, confirming our bedside evaluation. Intraocular pressure in the right eye was 70 mmHg. A CT scan confirmed the results. The patient was given rocephin, mannitol and diamox. The patient admitted that he had been robbed 2 weeks ago and knocked unconscious after a blow to the right eye. Unfortunately, the patient was admitted for enucleation surgery the next day.

Ocular ultrasound is being utilized with increasing frequency in the Emergency Room with high sensitivity and specificity for retinal detachment. This technique is easy to learn and adapted quickly for difficult eye exams where fundoscopy can be unreliable and can triage situations where emergency intervention is required.



Retina detachment and lens dislocation

15

SYNCOPE IN THE "SOUTH"

S. Boyapati, S. Kanikireddy, P. Bass *LSUHSC-Shreveport, Shreveport, LA.*

Case Report: INTRODUCTION: Sarcoidosis is an idiopathic inflammatory disease characterized by presence of non caseating granulomas in multiple organs. It can involve any organ of the body the most common being lung. Cardiac sarcoidosis is an uncommon yet a serious manifestation of sarcoidosis seen in 5% of cases leading to conduction problems. Sarcoidosis is relatively common in southeastern states especially among African American population.

CASE PRESENTATION: Patient is a 45 year old AAF with history of sarcoidosis, diagnosed ten years prior presented after a syncopal episode. She reported dizziness, palpitations and generalized weakness for one month. Fifteen days prior to admission patient was evaluated and the symptoms are attributed to uncontrolled hypertension and her medications were adjusted. But her symptoms continued to worsen and she went to local ER and was

diagnosed to have atrial fibrillation and was started on Coumadin. Initial work up in our facility including EKG was normal. Patient was admitted to telemetry. Echocardiogram revealed no abnormalities. However during the hospital course patient had repeated episodes of sinus pauses and occasional sinus tachycardia. After thorough evaluation symptoms were attributed to cardiac involvement secondary to sarcoidosis. Eventually, pacemaker was implanted and patient remained symptom free during the hospital stay.

DISCUSSION: Incidence of sarcoidosis is 10.9 in whites and 35.5 in African Americans per 100,000. Recent theories showed that African Americans with HLA-DR 11, 12, 14, 15, and 17 are more prone to develop sarcoidosis. The pathology is formation of noncaseating granulomas in response to an exaggerated immune reaction mediated by T-helper cells. Increased IgM & hyperglobulinemia against various infectious agents is also seen. Cardiac sarcoidosis is a rare complication which manifests with symptoms varying from benign arrhythmias to fatal ventricular fibrillations. ECG, Holter monitor, 2D Echo, CT scan, MRI are some of the diagnostic measures that can be used based on individual clinical scenarios. Cardiac biopsy is the gold standard for diagnosis but not generally recommended for diagnostic purposes. Depending on clinical scenario and severity of symptoms treatment varies from oral steroids to surgical intervention.

Pediatric Clinical Case Symposium

1:00 PM

Thursday, February 25, 2010

16

SUSPECTED TRAUMA IN COMATOSE CHILD FOUND TO BE BACLOFEN POISONING

A. Gardner, J. Byrnes, M. Moss, L. James *University of Arkansas for Medical Sciences, Little Rock, AR.*

Case Report: We report a case of baclofen poisoning in a previously healthy 23 month-old boy who presented after a witnessed ground-level fall in which his head struck a bookshelf. He immediately stood and began to cry, then became flaccid and unresponsive when picked-up by his father. Upon arrival at a local hospital 20 minutes later, the child's exam was consistent with brain death except for minimally reactive pupils and intermittently reactive corneal reflexes. Cough, gag, spontaneous respiratory effort, response to painful stimuli, and deep tendon reflexes were absent entirely. He was intubated and transported to a tertiary pediatric center where he continued to require mechanical ventilation. All neuroimaging and routine laboratory studies were normal. EEG initially demonstrated a burst suppression pattern; however, within 24 hours of admission this completely resolved and normal sleep patterns were observed. He remained hemodynamically and metabolically stable. Extensive questioning of the family revealed no history of drug or chemical exposure. Routine toxicology testing was negative. After two days of supportive management, he returned to his baseline neurologic function and was extubated. He was discharged home after four days in the hospital. The results of comprehensive urine toxicology testing later revealed moderate levels of baclofen. Subsequent investigation failed to reveal a source for the medication.

Baclofen is an orally active GABA-mimetic agent and a common antispasmodic. It is frequently the treatment of choice in spastic cerebral palsy because it is less sedating than other drugs used to treat muscle spasms. The adverse effects associated with baclofen poisoning have been well-described in the literature. However, less data is available in children and the duration of effects has not been well-described. A handful of baclofen poisoning cases in children have been reported, but to our knowledge they all presented with a known or strongly-suspected history of baclofen ingestion. This case highlights the difficulties encountered in pediatric poisonings and the limitations of routine toxicology screening. Baclofen overdose should be considered in the differential diagnosis of children presenting with coma, respiratory depression, and normal neuroimaging and laboratory studies.

17

THE APNEIC PATIENT: AN INTERESTING PRESENTATION OF PYLORIC STENOSIS

A. Koehler^{1,2}, L. Campion^{1,2} *¹UAMS, Little Rock, AR and ²Arkansas Children's Hospital, Little Rock, AR.*

Case Report: A 27 day-old ex 36wk Caucasian boy presented to Arkansas Children's Hospital Emergency Room with a 2 week history of apneic events which were becoming increasingly frequent. He had been placed on an apnea monitor by his primary care provider 5 days prior to visit. In the 48 hours prior to presentation, the patient had more than 100 recorded events lasting longer than 20 seconds. A venous blood gas and basic metabolic panel were obtained and showed a pH of 7.60, PCO₂ of 40.6mmHg, HCO₃⁻ of 39mmol/L, K⁺ of 3.1 mmol/L, and Cl⁻ of 81mmol/L.

In obtaining further history, mother reported 1 week of frequent, non-projectile, non-bilious vomiting which she attributed to "a stomach bug" that had improved. An abdominal ultrasound was obtained and showed a pylorus with a length of 15 mm and thickness of 3.5 mm. The surgical service was consulted and the patient was admitted for fluid resuscitation and electrolyte management. The patient's apneic events became less frequent as electrolytes and pH were corrected. Patient was taken to OR on HD #2 for laparoscopic pyloromyotomy. Patient's post-operative course was relatively uneventful. Patient was discharged home on Hospital day 4.

Pyloric stenosis is the most common cause of metabolic alkalosis in infancy. It is classically described as projectile vomiting, dehydration, and metabolic alkalosis at 3–4 weeks of life. While projectile vomiting is often the most striking symptom, it has been reported as absent in as many as 30% of cases in some series. Metabolic alkalosis is a known cause of apnea as the elevated pH decreases the patient's respiratory drive. These symptoms resolve as the alkalosis corrects.

This patient presented an interesting case as the hallmark symptom of Pyloric Stenosis - vomiting (projectile or otherwise) - was of only minimal concern to the patient's mother and the significant quantity of it was only elicited once the laboratory data provided more questions than answers. This case provides a reminder that a diagnosis cannot be excluded just because it does not fit the classical criteria and that a thorough history with a complete and in depth review of systems is crucial, particularly when dealing with multi-system pathology.

18

IVIG VERSUS HIGH DOSE STEROIDS IN THE TREATMENT OF ACUTE DISSEMINATED ENCEPHALOMYELITIS

L. Rhodes, J. McLendon, B. Toole, B. Harden *UAB, Birmingham, AL*

Case Report: We report a series of three pediatric patients with ADEM who showed clinical improvement only after the administration of intravenous immunoglobulin (IVIG). The first patient is a 7 year old white male who presented to the emergency department with a five day history of headache, three day history of fever, and one day history of difficulty walking. Following admission, the patient's mental status worsened, he became aphasic, developed an altered mental status, and could not stand up. Cerebral spinal fluid (CSF) analysis revealed 27 WBC, 0 RBC, 56 Glucose and 33 protein. The patient was initially treated with cefotaxime, vancomycin and acyclovir for concern of meningoencephalitis. All CSF and blood studies sent for tick born illnesses, HSV, arboviruses and bacterial infection were negative. An MRI showed regions of hyperintensity within the basal ganglia, subcortical white matter and within the cortex consistent with ADEM. The patient received five days of high dose intravenous steroids and failed to show clinical improvement. After completion of steroid therapy, the patient was given 1 gm/kg of IVIG for two days. During this time, the patient showed significant clinical improvement. He regained the ability to talk, he became oriented to person and place, and he was able to bear weight and ambulate. Patient two and three presented with similar neurological deficits and underwent the same initial workup as patient one above. CSF studies showed an elevation in leukocytes and workup for infectious etiologies was unremarkable. MRI on both patients was consistent with ADEM. Patient two was initially treated with high dose steroids for five days and failed to show clinical improvement. He subsequently received two days of IVIG with rapid improvement in symptoms. Patient three was treated with IVIG only on day 3 of admission. He started demonstrating improvement immediately after the first dose. All three patients failed to show clinical improvement until IVIG was administered.

High dose steroids are currently the initial treatment choice for patients diagnosed with ADEM. This case series provides evidence for the use of IVIG initially in the treatment of ADEM. Further research is needed to determine the superiority of IVIG over steroids in the initial treatment of ADEM.

19

LAZY ARM RACY INFANT

JS. Hothi, R. Philip, M. Lucas, G. Balasubrahmanyam *East Tennessee State University, Johnson City, TN*

Case Report: 11 M/O white female was referred to the pediatric neurology clinic with progressive inability to use her painful left arm and thought to be secondary to Erb's Palsy. At 3 months of age mother had noticed the infant cried when she lifted her up under her arms. Maternal lifting pattern was changed. At 10 months of age the infant slept restlessly and the left arm was intermittently limp. This progressively worsened until the infant completely stopped crawling and refused to use the limp left arm. ROS: negative PMH: FT AGA NSVD no traumatic delivery, normal growth and development (speech, personal-social) except motor development (can sit without support, but not crawl or use her left arm) O/E : T : 98F HR:115 BP:87/62 Wt : 9.8 kg HC:44.2cm No CR distress. Examination was normal except for left upper arm. Left arm had areflexia with flaccid tone, decreased muscle bulk, diminished strength, and tenderness to palpation consistent with painful monoplegia and transient progressive limb paralysis. X-ray of the left upper arm and shoulder was normal. Consequently, an MRI of the left brachial plexus and C-spine showed an enhancing mass expanding the neural foramen of C5-C6 extending along the left brachial plexus into the left axillary region consistent with multiple neurofibromas. Neurosurgery performed a decompressing laminectomy of C4-5-6-7 and partial excision on C6 epidural mass. Pathology results confirmed atypical teratoid rhabdoid tumor. Emergency chemotherapy with ifosfamide and etoposide was initiated along with decadron.

This case emphasizes the importance of ROS and developmental screening at well child visits. The classic Erb's palsy is usually present in proximity to traumatic birth injury, recovery can be detected at 2 weeks, and full recovery occurs within 4–6 months in the majority of cases. In this particular case, onset was at three months and progressively worsened for 9 months. A prompt evaluation for secondary causes is always warranted in such cases to rule out tumor, trauma, abuse or septic arthritis. This case reiterates that any development regression is a red flag that needs further emergent evaluation.

20

LETHAL RHABDOMYOLYSIS AND STAPHYLOCOCCUS AUREUS SEPSIS IN A HEALTHY TEENAGER

CL. Freeman, KC. Clement, X. Garcia, JG. Wheeler, NS. Harik *University of Arkansas for Medical Sciences/Arkansas Children's Hospital, Little Rock, AR*

Purpose of Study: To describe rhabdomyolysis as a presenting symptom of methicillin resistant *Staphylococcus aureus* (MRSA) sepsis.

Methods Used: Chart review, autopsy review, literature review, and bacterial analysis.

Summary of Results: A previously healthy 16 year old African American boy presented to our hospital with a working diagnosis of acute renal failure (ARF) secondary to rhabdomyolysis. Five days prior to admission, he complained of right hip pain. Three days before admission, he sought outpatient care for continued complaints of pain extending from the right hip into the hamstring area. He was treated with steroids, muscle relaxers, and pain medications. The day before admission, he was taken to an outside hospital and found to have ARF with elevated BUN (70mg/dL) and creatinine (6 mg/dL). His CPK level was elevated at 12000 IU/L and urinalysis showed large blood but only 3–5 red blood cells/HPF. Rhabdomyolysis was diagnosed clinically and he was transferred to our facility. Upon admission, he had poor perfusion, decreased urine output and unstable vital signs. Echocardiogram revealed diminished cardiac function (shortening fraction of 14%). He was begun on vancomycin and meropenem for presumed sepsis. Despite aggressive treatment and extracorporeal cardiopulmonary support (ECMO), he died less than 24 hours after admission secondary to fatal cardiac arrhythmias and uncontrollable hyperkalemia even with dialysis. Multiple blood cultures grew MRSA within hours of being drawn. Autopsy revealed microabscess formation within the skeletal muscle, heart, and lungs secondary to MRSA. Review of the literature revealed few published cases of rhabdomyolysis and MRSA sepsis in immunocompetent patients, and only one was in a child. Molecular analysis of this strain of MRSA is underway to determine if there are virulence factors present that may explain why his infection was so aggressive and atypical.

Conclusions: While MRSA sepsis is a well recognized entity, rhabdomyolysis as a presenting symptom/complication in children is not well described in the literature nor has it been seen in our clinical practice. No genetic assessment of the MRSA strains associated with rhabdomyolysis has ever been performed.

21 SEVERE HEMOLYSIS AND METHEMOGLOBINEMIA IN A PATIENT WITH LOXOSCELISM: A CASE REPORT AND REVIEW

C. Ranallo, H. Farrar, S. Pasala *UAMS, Little Rock, AR.*

Purpose of Study: We report the case of a 1 year old with systemic Loxoscelism manifesting as fever, hemolytic anemia, methemoglobinemia, necrotic wound, elevated liver enzymes, and elevated CPK. Systemic manifestations of *Loxosceles reclusa* are important to recognize and include in the differential for hemolytic anemia.

Methods Used: To report a case of a toddler with Loxoscelism and methemoglobinemia, in which early recognition and aggressive management resulted in a favorable outcome.

Summary of Results: A 1 year old presented to PCP for low grade fever and red lesion on right shoulder, diagnosed as cellulitis. The next day the mother found with hematuria. At the local ED, an IO was placed and she was given a dose of rocephin, and then transferred emergently to ACH. Upon arrival she was noted to be pale, jaundiced, and irritable with poor saturations on nasal canula. Initial lab revealed HCT 9.9, Tbil 6.9, AST 969, CPK 447, positive blood on UA but no RBC's, and hemocult neg. Evaluation on admission of her cellulitis demonstrated a 3 cm erythematous lesion with 3 mm area of central necrosis, thus Loxoscelism rose to the top of the differential. The hemolysis resolved over several days after serial transfusions and alkalization of fluids.

On day 1, after the first transfusion she was noted to appear cyanotic. A methemoglobin was obtained, which was 9.9. Several events were considered as a possible explanation for methemoglobinemia in this case including the Bactrim at PCP, lidocaine given for IO placement, extreme oxidative stress of hemolysis, enzymatic defect, other toxic exposures in the home including moth balls. After consulting toxicology, methylene blue was given.

Although severe systemic symptoms are relatively rare, 1.2% of bites, the ability to anticipate and recognize early symptoms is important for reducing morbidity. Early recognition of methemoglobinemia in this patient given the severity of anemia was important for reducing morbidity.

Conclusions: Severe systemic manifestations of *Loxosceles reclusa* bites are rare but serious. Severe hemolysis and methemoglobinemia has not been previously described together in conjunction with Loxoscelism.

22 A CASE OF NOT SO SIMPLE VOMITING

Y. Gardiner², K. Monroe¹ *¹Univ of Alabama, Birmingham, AL and ²Children's Hospital, Birmingham, AL.*

Purpose of Study: HISTORY 5 month old previously healthy male presented with 3 days of nbnb emesis. no fever. no diarrhea. last normal bm was 3 days prior. (no bms in 3 days). no fever no cough no other symptoms. He had been seen in ED on day one of illness for an episode of gagging and "making a funny sound." At that visit he had a normal exam and tolerated oral fluids well and was discharged home. Day two, patient was seen again for vomiting (nbnb) again had normal exam but had continued vomiting and was given IV fluids, and tolerated oral fluids well in the ER and was discharged home.

Methods Used: PHYSICAL EXAM: afebrile, triaged as "green" meaning non urgent. upon exam in room, noted to be lethargic and vomiting (nbnb). Patients was very fussy not wanting to be held or touched. ncst peril comi op dry lungs clear, cardiac exam with minimal tachycardia abd soft with no masses rectal grossly bloody.

Summary of Results: RADIOLOGIC EVALUATION: abdominal plain film: dilated loops of bowel with decreased air distally. Ultrasound positive for intussusception.

HOSPITAL COURSE: air enema reduced intussusception and patient was admitted for overnight observation.

Conclusions: Intussusception can be a difficult diagnosis masquerading as gastroenteritis at times. Diagnosis requires a high index of suspicion. This case presented three times before diagnosis was obvious.

23 CRANIAL IMPALEMENT OF AN ALL TERRAIN VEHICLE BRAKE HANDLE IN A HELMETED CHILD

G. Long², TM. Thompson^{1,2}, J. Graham¹ *¹UAMS, Little Rock, AR and ²UAMS, Little Rock, AR.*

Case Report: An 8-year-old boy arrived via helicopter from the scene of an ATV (all-terrain vehicle) accident. The patient was helmeted and riding the ATV for the first time. The machine rolled over; a brake handle impaling the boy's skull superior to the left ear. Medics disassembled the brake from the ATV, requiring 30 minutes. The patient was stable in transport and he arrived at the hospital with a Glasgow Coma Scale of 15.

Examination revealed a 7 inch metal handle protruding above his left ear, angled through the temporomandibular joint toward the oropharynx. The patient had difficulty opening his mouth, with the brake moving with his attempts to open his mouth. He had a normal neurological exam. The only other abnormal finding was a right knee effusion and ecchymoses.

His past medical history included asthma and a recent infection of the right knee. He took no medications. His immunizations were up to date and had an allergy to penicillin.

He was given fentanyl and ondansetron for pain and nausea. Soon after, he developed hypoxia (oxygen saturation 55%). His hypoxia corrected with bag valve mask ventilation and 0.01mg of naloxone.

Skull xrays demonstrated the foreign body, but no calvarial or facial fractures. Computed tomography (CT) showed extensive subcutaneous emphysema in the neck with fractures of the left pterygoid plates but no evidence of brain injury. CT angiography of the neck was normal.

The patient was transferred to the operating room for airway placement via kaleidoscope, followed by manual removal of the handle from his skull without difficulty. He was discharged on day three with a normal neurological examination.

This case presents a unique injury pattern; demonstrating the danger inherent in allowing a child with immature judgment and motor skills to operate an ATV. It is also unique in that the brake handle impalement was an isolated injury. Although helmets have been shown to reduce severity of head injury in ATV incidents, this case shows that not all ATV-related head injuries can be prevented by helmet use. Finally, this case vividly demonstrates the danger of ATV operation by children.

24 DILATED CARDIOMYOPATHY: AN UNUSUAL INITIAL PRESENTATION OF HYPOPARATHYROIDISM IN AN INFANT

KP. Patra, RD. Jackson, E. Kiel, S. Reddy *LSUHSC, Shreveport, LA.*

Case Report: Hypocalcemia is a great masquerader. It is a known, albeit rare cause of reversible cardiomyopathy. A very few anecdotal cases of cardiac failure attributed to hypoparathyroidism have been reported; however, all of them had a very late age of presentation. We herein report a case of dilated cardiomyopathy as an initial manifestation of hypoparathyroidism. A 35 day old term male infant with unremarkable birth history presented with tachypnea, excessive crying, and diaphoresis while feeding over the previous 2 weeks. He had a history of poor weight gain since birth. On examination, he was afebrile, tachycardic, tachypneic and hypotensive. He had prolonged capillary refill, feeble pulses, gallop cardiac rhythm, a 3/6 holosystolic murmur with radiation to left axilla, bibasilar rales, and hepatomegaly. Chest Xray showed cardiomegaly. He was initiated on intravenous fluids and dobutamine; however, there was no improvement. He was intubated for increased work of breathing and started on mechanical ventilation. EKG showed biventricular hypertrophy with strain pattern and prolonged QTc interval (0.52 s). Metabolic profile showed hypocalcemia (3.9 mg/dl), hyperphosphatemia (15.2 mg/dl) and normal magnesium. He was started on intravenous calcium chloride infusion. ECHO revealed normal anatomic heart, severe dilated cardiomyopathy and 3+ mitral regurgitation. Ejection fraction was reduced (28%). A dramatic hemodynamic improvement was noted with normocalcemia. Dobutamine and mechanical ventilation were weaned off in 12 hours. He was started on oral calcium, cholecalciferol, diuretics, captopril, and digoxin. He was switched to a low phosphorus formula (Similac 60/40). Work up revealed an undetectable parathyroid hormone (PTH) level. Fluorescent In Situ Hybridization probe for 22q11 microdeletion was negative. Maternal hyperparathyroidism was ruled out. At discharge, he was feeding well with steady weight gain. Repeat ECHO

showed improvement in ejection fraction (57%) and 2+ mitral regurgitation. He was discharged on calcium glubionate, cholecalciferol, diuretics, and digoxin. Digoxin and diuretics were discontinued on follow-up. Infantile hypoparathyroidism will be discussed.

25

AN ATYPICAL PRESENTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS

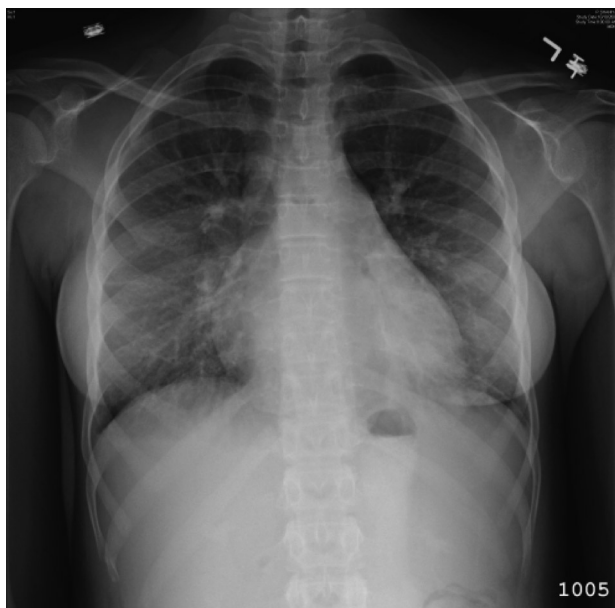
L. Gonsette, J. El-Dahr *Tulane University Hospital & Clinic, New Orleans, LA.*

Purpose of Study: Recognize the varying clinical presentations and differential diagnosis of Systemic Lupus Erythematosus.

Methods Used: 14 year old girl presented with progressive proximal muscle weakness and fatigue after a viral infection one month ago. Workup revealed rhabdomyolysis & hyperuricemia supporting post viral sequelae but incidentally had pancytopenia and small bilateral pleural effusions. Bone marrow biopsy demonstrated no evidence of malignancy. Serological markers for rheumatological disorders revealed Systemic Lupus Erythematosus.

Summary of Results: SLE may not always present with the classic cutaneous, arthritic and nephrologic manifestations and often mimic other illnesses making diagnosis challenging and protracted.

Conclusions: SLE is a multiorgan autoimmune disorder that often presents with protean manifestations.



26

HIRSCHSPRUNG'S DISEASE IN AN EXTREMELY PRETERM INFANT. A CHALLENGING DIAGNOSIS

R. Bhat, J. Kelleher, RA. Dimmitt, C. Coghill *University of Alabama at Birmingham, Birmingham, AL.*

Case Report: A male infant was born at 23 completed weeks gestation by spontaneous vaginal delivery with a birth weight of 520 grams. He had Apgar scores of 3 and 6 at 1 and 5 minutes respectively. He was initially managed in the delivery room with intubation and surfactant administration. He subsequently remained ventilator dependent for the entire 5 months of his life with bronchopulmonary dysplasia. He failed numerous attempts at enteral feeding as characterized by periods of abdominal distention and increased gastric residuals. Therefore he was transferred from the birth institution to the Children's Hospital of Alabama at 4 months of age for further management.

Further attempts of enteral feedings were subsequently unsuccessful. A barium enema was performed at 41 weeks corrected gestational age. This

revealed saw tooth irregularity of the mucosa of the distal rectum, a transition zone at the recto-sigmoid junction and a very dilated proximal colon. A diagnosis of Hirschsprung's disease was considered. Acetyl cholinesterase staining performed on a rectal biopsy confirmed Hirschsprung's disease. Two weeks later an exploratory laparotomy with a sigmoid colectomy was performed. The histopathology of the resected sigmoid colon confirmed the findings of the previous biopsy as consistent with a diagnosis of Hirschsprung's disease. The infant remained ventilator dependent throughout the subsequent three post-operative weeks. Enteral nutrition was commenced and gradually increased over a period of ten days. In spite of tolerating this initial feeding advance, he subsequently developed an overwhelming sepsis with refractory metabolic acidosis. He died following three episodes of cardiopulmonary arrest.

There are few case series in the medical literature that describes Hirschsprung's disease in low birth weight infants. However a case of Hirschsprung's disease in a 23 week premature infant has not been described to date. This case that we have highlighted is unique and serves as a solemn reminder to clinicians when considering the differential diagnosis of feeding intolerance in ELBW infants.

Case Reports in Cardiovascular Medicine

2:00 PM

Thursday, February 25, 2010

27

A CASE OF GERBODE DEFECT AND PNEUMOCOCCAL ENDOCARDITIS: A CHICKEN OR EGG CONUNDRUM

KP. Patra, A. Wu, E. Kiel *LSUHSC, Shreveport, LA.*

Case Report: A Gerbode defect is a rare ventricular septal defect (VSD) with left ventricle to right atrium (RA) communication. It is usually congenital. We herein report a unusual case of Gerbode defect associated with Pneumococcal endocarditis. A 12 year old previously healthy female presented with a history of sore throat, dizziness and oliguria. On examination, she had fever, pallor, tachycardia, hypotension and a 2/6 pulmonary systolic murmur. Investigations revealed anemia, leucocytosis and elevated acute phase reactants. Blood culture yielded Penicillin-sensitive *Strep. pneumoniae*. ECHO on hospital day 2 showed a wind sock lesion in RA consistent with Gerbode defect closure versus possible vegetation. Despite antibiotics and subsequent negative blood cultures, she had persistent fever. ECHO on Day 5 showed Gerbode defect with shunt to RA and no obvious vegetations. On Day 7, she complained of dyspnea and chest pain. On exam, she had a pericardial rub and a to-and-fro murmur. ECHO showed significant pericardial effusion, Gerbode defect and severe aortic insufficiency. She was transferred for surgery. *Pneumococcus* accounts for about 4% cases of infective endocarditis (IE) in children. The mean age of presentation is 4 years. It has a high case fatality rate and management involves a combined medical and surgical approach. The work up to rule out any predisposing factors for pneumococemia (hypocomplementemia, asplenia, rheumatologic disorders) was negative. The mechanism of septal perforation in our case can only be hypothesized. Her VSD could be congenital which had closed with a septal aneurysm and then perforate secondarily due to bacteremia. It could also result from bacterial invasion of an intact septum. Gerbode defects are associated with a 4 times higher risk for IE; however, AHA 2007 guidelines do not recommend prophylaxis. Should such defect if detected entail IE prophylaxis is a question to ponder. Despite such invasive endocarditis, she didn't meet Duke criteria until day 7 when she satisfied 'possible' IE criteria. Recent studies have suggested redefining Duke classification. She later on developed surgical complications including complete heart block and valve dehiscence. Could these complications be averted had she met the diagnosis for IE earlier, remains an interesting speculation.

28

REVASCULARIZATION AFTER A SMALL INFERIOR MYOCARDIAL INFARCTION WITH COMPLETE HEART BLOCK

R. Nagarakanti¹, M. Stellingworth², MJ. Ali¹, DL. Glancy¹ *¹Louisiana State University School of Medicine, New Orleans, LA and ²University Medical Center, Lafayette, LA.*

Case Report: Complete atrioventricular block (CAVB) complicates acute inferior wall myocardial infarction (AIMI) with increased morbidity and mortality. We describe a patient with an inferior MI in whom successful PCI was effective in reversing persistent CAVB, thus avoiding implantation of a permanent pacemaker (PPM).

CASE: A 51-year-old man was admitted with 2 hours of epigastric pain after 3 days of worsening 5–10 minute episodes of pain. History was significant for hypertension, heavy smoking and coronary artery disease with angioplasty of the right coronary artery (RCA) 7 years ago. Medications included aspirin, atenolol, enalapril and pravastatin.

On admission, temp was 99.7°F, pulse, regular @ 38 bpm, and BP, 106/57 mm Hg. Heart sounds were diminished with no murmurs or gallops. Laboratory tests showed leukocytosis and elevated cardiac markers (CPK 156 U/L, CK-MB 4.8 NG/ML, and Troponin 2.9 NG/ML). Troponin peaked at 4.65 NG/ML. Initial electrocardiogram (ECG) demonstrated CAVB, no ST elevation, and T-wave inversion in leads II, III and aVF. Pain resolved spontaneously, and intravenous heparin and eptifibatide were started. Atenolol was stopped. He underwent coronary arteriography and transvenous pacemaker placement with the rate set at 60 bpm. Coronary arteriography demonstrated sub-total occlusion of the mid RCA and 30–40% stenosis of left anterior descending and left circumflex coronaries. He underwent PCI with bare-metal stent placement in the RCA. On hospital day 2, the pacemaker rate was lowered, and the ECG demonstrated sinus rhythm (SR) with first degree AV block and Q waves in the inferior leads. Metoprolol 12.5 mg twice daily was started, and he remained in SR with a heart rate of 60–75 bpm. The pacemaker was removed. He was discharged on hospital day 3 on aspirin, clopidogrel, metoprolol, statin and an ACE inhibitor. In clinic one week later he was asymptomatic in sinus rhythm.

CONCLUSION: Rarely, CAVB occurs in patients with a small AIMI. In selected patients with AIMI and CAVB, PCI may be considered as a treatment option before recommending PPM implantation.

29

CONCURRENT ACUTE CORONARY SYNDROME AND ISCHEMIC STROKE FOLLOWING MULTIPLE BEE STINGS

W. Dechyapirom, C. Cevik, K. Nugent *Texas Tech University Health Sciences Center, Lubbock, TX.*

Case Report: Purpose of Study: Local and systemic reactions after bee stings are common, but there are few reports of severe complications, such as acute coronary syndrome and stroke. We report the first case of cerebral infarction and non-ST-segment myocardial infarction after multiple bee stings.

Methods Used: We used the PubMed database to search bee stings and stroke and/or acute coronary syndrome. We also reviewed the relevant references in the papers from this search. We compared these data with our case to find the common manifestations, pathophysiology, and the optimal treatment.

Summary of Results: A 64-year-old man was stung by 200 bees. The stingers were removed in the emergency department, and he was treated with steroids, opioid and antiemetics. He had itching but no other problems. Sixteen hours later he had left side weakness and chest pain. He was treated with tPA two hours after the onset of his neurological symptoms. Brain magnetic resonance imaging showed a large right middle cerebral artery ischemic stroke and 2–3 mm midline shift. Cardiac enzymes were elevated (peak troponin-1.48ng/ml); the ECG showed no ST elevation. Neurological exams improved daily, and the patient was transferred to a rehabilitation facility. We found four cases of stroke and three cases of acute coronary syndrome that followed bee stings. All the patients with stroke had typical neurologic deficits and were treated with steroids; none of them received thrombolytic therapy. None of them recovered fully; while our patient had only minimal residual deficits at transfer.

Conclusions: We report the first case with both syndromes in the same patient and suggest the following mechanism for injury. Our patient did not have an acute allergic reaction and did receive steroids which should prevent a delayed reaction. The bee venom likely induced a toxic reaction with vasospasm and thrombosis, perhaps involving occult plaques in the cerebral and coronary circulation. He was treated with thrombolytic therapy and had clinically significant improvement over 24 hours. The fact that our patient responded to this treatment does not establish this mechanism but does suggest that stroke after multiple bee stings should be treated with steroids and thrombolytic therapy.

30

ATRIAL AND VENTRICULAR ARRHYTHMIAS IN A WOMAN WITH PROLONGED QT_c, HYPOKALEMIA, HYPOMAGNESEMIA AND A METABOLIC ALKALOSIS

AA. Adeboye, BJ. Borkowski, KT. Weber *University of Tennessee Health Science Center, Memphis, TN.*

Case Report: Purpose: In 1966, Gitelman reported on two sisters who had chronic dermatitis, episodic mild muscle weakness, hypokalemia and hypomagnesemia due to a primary renal tubular hypokalemic metabolic alkalosis. The QT_c interval can be prolonged in association with hypokalemia and hypomagnesemia and therefore these patients are susceptible to atrial and/or ventricular arrhythmias. Herein we report on a woman with the Gitelman syndrome, who not only had these electrolyte abnormalities and QT_c prolongation, but also premature atrial and ventricular contractions.

Case Report: A 62-year-old African-American woman was hospitalized in August, 2009, with breathlessness upon minimal exertion, orthopnea, intermittent muscle weakness, and bilateral lower extremity edema. She was not receiving any medications, however, her mother and grandmother were taking potassium supplements. Physical findings included chronic erythematous dermatitis of the anterior thorax. Jugular venous distention, bibasilar rales, and a displaced apical impulse with ventricular gallop sound led to a presumptive diagnosis of congestive heart failure albeit of uncertain etiology confirmed by radiographic cardiomegaly and pulmonary congestion. Normal sinus rhythm, QT_c 481 ms, and ectopic atrial and ventricular beats were present on ECG. Pertinent laboratory findings: hypokalemia (2.7 mEq/L), hypomagnesemia (1.5 mg/dL) and bicarbonate (29 mEq/L). Despite oral supplementation, these electrolyte abnormalities failed to correct leading to further evaluation: transtubular potassium gradient 10.4; urinary Ca²⁺/creatinine ratio 0.06; and fractional excretion of filtered Mg²⁺ 7.4%. The diagnosis of the Gitelman syndrome was made. Resting plasma renin 8.03 ng/L and aldosterone 13.2 ng/dL. Intravenous supplementation corrected her serum electrolytes, which were then sustained with spironolactone while QT_c was normalized (440 ms) and ectopic beats resolved.

Conclusion: Hypokalemia and hypomagnesemia, together with a metabolic alkalosis, are frequently associated with QT_c prolongation. Not infrequently patients presenting with this metabolic/ECG profile will have an inheritable renal tubular disorder, such as the Gitelman syndrome, and a susceptibility to cardiac arrhythmias.

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CARDIAC AMYLOIDOSIS IN A 47-YEAR-OLD MAN

H. Franqui-Rivera, H. Banchs-Pieretti, M. Garcia-Palmieri *University of Puerto Rico, Rio Piedras, PR.*

Case Report: A 47-year-old man with no systemic illnesses presented to the emergency room because of shortness of breath at rest. He described a three-month history of dyspnea on exertion, which worsened to shortness of breath at rest. He also complained of paroxysmal nocturnal dyspnea, orthopnea, leg edema, and increased abdominal girth. Past medical and family history were unremarkable. Admitted occasional alcohol consumption but denied cigarette smoking or illicit drug use. On physical examination, blood pressure was 81/53 mmHg and heart rate 103 bpm. There were diffuse inspiratory wet crackles with bilaterally decreased breath sounds at lung bases, along with decreased tactile fremitus. Auscultation of the heart revealed a 2/6 systolic murmur at the left upper sternal border and a fourth heart sound (S4). Grade 2/4 edema of the lower extremities was noted. Electrocardiogram disclosed low voltages. A two-dimensional echocardiogram demonstrated a severely hypertrophied left ventricle with speckled appearance and a restrictive transmitral inflow filling pattern. Left ventricular ejection fraction was 67%. Laboratory analyses revealed a serum creatinine of 1.25 mg/dL (CrCl 67 mL/min/1.73 m²), 3+ proteinuria, and mildly elevated liver enzymes. Serum and urine protein electrophoresis revealed a monoclonal band consisting of kappa light chains. Bone marrow biopsy was negative for multiple myeloma but showed increased plasma cells. An endomyocardial biopsy demonstrated multiple extracellular, eosinophilic, amorphous hyaline deposits. Congo-red stain revealed apple-green birefringent deposits, consistent with cardiac Amyloidosis. The patient has been treated with thalidomide plus prednisone, as well as the usual therapy for heart failure. The patient is currently awaiting autologous stem cell and heart transplantation. Cardiac amyloidosis is a rare cause of restrictive cardiomyopathy. It may be seen in up to 25% of patients with light chain deposition disease,

which in turn is usually associated with lymphoproliferative disorders, as in this case.

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COMPLETE LEFT CORONARY ARTERY ATRESIA IN ASYMPTOMATIC ADULT. A CASE REPORT

I. Hameed, A. Reddy, F. Wilklow, A. Anwar, LP. O'Meallie *Tulane University and Heat Vascular Institute, New Orleans, LA.*

Case Report: Objective: Left coronary artery atresia is an extremely rare coronary anomaly and mainly described in pediatric age group in which the proximal left main trunk ends blindly and blood flows from the right coronary artery to the left via small collateral arteries and retrogradely in at least one of the left-sided arteries. We are describing a case report of a complete absence of left coronary system in asymptomatic adult.

Case report: 68 year old male was referred to our center for coronary angiogram after an abnormal nuclear stress test. Patient was completely asymptomatic and was scheduled for an intermediate risk surgery. His laboratory findings were within normal limit and EKG was unremarkable. His angiograms showed a gigantic right coronary system and complete absence of left coronary system except tiny blind bud at the site of left coronary sinus. His left ventricle (LV) function was grossly normal. Given the absence of retrograde flow on left side, normal LV function and abnormal stress test; CT angiography was performed which showed similar results. Patient did fine after non-cardiac surgery.

Discussion: The incidence of all coronary anomalies is low in general population ranging from 0.46% to 1.55%. However the incidence of true LM coronary atresia is unknown; current literature review showed 33 case reports. Musiani et al reviewed 28 case reports, 15 were pediatric and 5 of these cases also had associated cardiac anomaly. Majority of patients with LM coronary atresia were symptomatic (syncope, dyspnea, infarction, ventricular tachycardia, sudden death) and underwent coronary artery revascularization via one or more saphenous vein or mammary artery grafts to the left-sided arteries. Our patient was completely asymptomatic, with absence of retrograde flow to left side and normal left ventricular function, and was managed without surgery.

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ATRIAL AND VENTRICULAR ARRHYTHMIAS IN A MAN WITH HYPERTENSION, HYPOKALEMIA, HYPOMAGNESEMIA AND METABOLIC ALKALOSIS

J. Yusuf, K. Ahmad, KT. Weber *University of Tennessee Health Science Center, Memphis, TN.*

Case Report: Purpose: Episodes of atrial fibrillation (AF) and ventricular arrhythmias can be precipitated during electrolyte disturbances, which include hypokalemia and hypomagnesemia with a metabolic alkalosis, and are often seen in association with a thiazide or loop diuretic. Herein, we draw attention to a patient with a history hypertension, paroxysmal AF, and these same electrolyte abnormalities, not related to diuretics, emesis or diarrhea, who had a documented recurrence of AF and the appearance of ventricular arrhythmias during his hospitalization.

Case Report: A 58-year-old African-American male with a history of hypertension and paroxysmal AF one year ago, presented in May, 2009 with a 2-day history of dyspnea and palpitations. He denied chest pain, vomiting or diarrhea, illicit drug use and was not taking prescribed or across-the-counter medications. BP 150/86, irregularly irregular central and peripheral pulses of 150 and 120 bpm, respectively, with a pulse deficit of 30 bpm. Lung fields were clear and a ventricular gallop sound was heard at the apex; there was no cyanosis, clubbing or edema. Serum electrolytes: K^+ 3.6 mEq/L; Mg^{2+} 1.8 mg/dL; and HCO_3^- 29 mmol/L with a tubular K^+ gradient of 3.8. Thyroid panel was normal. ECG revealed prolonged QTc of 558 ms and rapid atrial fibrillation/flutter for which he received intravenous diltiazem. On hospital day 3 he was found unresponsive with an idioventricular rhythm that later progressed to Torsades and from which he was successfully cardioverted. Hypokalemia and hypomagnesemia persisted despite oral electrolyte supplementation. Plasma renin activity was undetectable and an aldosterone: renin ratio of 44 led to the diagnosis of primary aldosteronism. Spironolactone provided control of both his hypertension and electrolytes and QTc was reduced to 440 ms, however, he remained in AF.

Conclusion: Although less well appreciated, primary aldosteronism is associated with an increased risk of adverse cardiovascular events, including

arrhythmias that can be precipitated by electrolyte abnormalities. This case underscores the need to consider Conn's syndrome in patients with hypertension who present with AF, hypokalemia, hypomagnesemia and a metabolic alkalosis.

Joint Poster Session

Adolescent Medicine and Pediatrics

5:00 PM

Thursday, February 25, 2010

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INCREASED ACCESS TO CARE IN A PEDIATRIC MOBILE HEALTH PROGRAM

R. Arnberger, E. Bellino, A. Olteanu *Tulane University School of Medicine, New Orleans, LA.*

Purpose of Study: The New Orleans Children's Health Project (NOCHP) is a pediatric mobile health program developed as a partnership between the Children's Health Fund and Tulane School of Medicine, Department of Pediatrics. NOCHP operates out of two state-of-the-art mobile units. One unit offers pediatric primary care services and the second one provides children and their families with mental health services. NOCHP provides services in four underserved communities in the Greater New Orleans area. Patient failure to adhere to scheduled appointments is a common problem in medical and mental health clinics. Chronic failure to attend medical or mental health appointments can affect the quality of treatment outcomes and the fiscal viability of the clinic.

Numerous studies have been conducted to examine the problem of non-adherence however, no studies have been conducted that document no-show rates of a mobile clinic. The mobile clinic model of care was originally developed in part as an attempt to reduce barriers to accessing quality and affordable medical care, thus improving adherence to quality care. NOCHP's model of care attempts to reduce numerous barriers to care that many patients experience in an inner city setting. These include inaccessibility to care due to location or lack of transportation, inability to pay, lack of insurance, and being undocumented.

Methods Used: NOCHP began internally tracking rates of adherence to scheduled appointments as a routine quality improvement measure in 2007. In 2008 and 2009, in an effort to improve access to care in our patient population, we began regularly contacting patients who failed to show to their scheduled appointments to assess the reasons why and to offer them the opportunity to reschedule their appointment.

Summary of Results: NOCHP began internally tracking rates of adherence to scheduled appointments as a routine quality improvement measure in 2007. In 2008 and 2009, in an effort to improve access to care in our patient population, we began regularly contacting patients who failed to show to their scheduled appointments to assess the reasons why and to offer them the opportunity to reschedule their appointment.

Conclusions: These results illustrate how a mobile clinic model of care can successfully reduce barriers to care as well as how to improve appointment adherence rates.

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AN UNUSUAL PRESENTATION OF CHOLECYSTITIS

TN. Cauley, I. Jubran *University of South Alabama, Mobile, AL.*

Case Report: A fifteen year old obese Caucasian female with a history of hypothyroidism and polycystic ovarian syndrome presented as a new patient in our clinic for follow up of a recent hospitalization. She was hospitalized due to a two week history of nausea and vomiting accompanied by left upper quadrant pain. Her hospitalization included an extensive workup, including an exploratory laparotomy which resulted in an appendectomy and an EGD which showed loss of vascular pattern in the stomach and three ulcers. Abdominal films revealed significant constipation. Serology revealed a current EBV infection. At the time of the follow up visit, the patient reported continued nausea with a decrease in frequency but no change in intensity which was unrelieved by antiemetics along with left upper quadrant pain worsening in intensity. She was having hard, irregular bowel movements. The patient was treated with various combinations of PPIs, H2 blockers, antiemetics, and stool softeners over the next few months with worsening of

the left upper quadrant pain including periods of exacerbation that lasted for a few hours during day and/or night. The episodes were associated with nausea and episodes of paleness followed by erythema of the upper back, chest, and face. Her bowel movements were now grayish in color. She had a five kilogram weight loss, had stopped all activities, and was participating in the homebound school program. The patient was being followed by two gastroenterologists, as well as psychiatry, and had received osteopathic manipulation for possible musculoskeletal etiologies. She had presented to the emergency department on multiple occasions and had multiple hospital admissions secondary to pain that was unresponsive to medications. Upon subsequent presentation to the emergency department, again secondary to pain, the patient underwent a HIDA scan which revealed significant inflammation of the gall bladder despite negative abdominal ultrasounds and a negative HIDA scan in the past. She was taken for endoscopic cholecystectomy the next morning. The patient has been without pain now for over a year and a half. This case illustrates an unusual presentation of what is usually thought to be a straightforward diagnosis. The location of her pain along with concomitant illnesses delayed her diagnosis and impaired her quality of life.

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CHILD WELFARE CASEWORKER & RESOURCE PARENT PERCEPTIONS & BARRIERS TO ACCESSING MENTAL HEALTH SERVICES FOR CHILDREN IN FOSTER CARE

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¹University of Oklahoma Health Sciences Center, Oklahoma City, OK and
²Oklahoma State University, Oklahoma City, OK.

Purpose of Study: The current study investigated how RP and CW currently access mental health services as well as their perceptions of and barriers to accessing mental health services.

Methods Used: CW and RP throughout Oklahoma were invited to complete online surveys assessing barriers and access to health care for children in foster care. CW and RP surveys were separate, but comparable in content. Survey content was developed through focus groups held with CW and RP and discussions among a collaborative panel of stakeholders: Child Welfare, Oklahoma Health Care Authority (OHCA), Oklahoma Department of Mental Health and Substance Abuse Services (ODMHASAS), Foster Parent Association, and a young adult who had "aged-out" of child welfare custody.

Summary of Results: Six hundred CW (56% of invitees) and 320 RP (28% of invitees) completed the survey during July-August 2008. The sample included CW from 84% of Oklahoma counties and RP from 68% of counties. Among various health service needs, mental health services were most frequently rated as the most difficult to access by RP and second most frequent by CW. Approximately 27% of RP stated mental health services were not currently available in their hometown. CW generally reported that mental health therapy services were available; however, 24.1% denied availability of psychotropic medication management and 20.1% denied availability of psychological testing in or near their county. Both RP and CW expressed significant concerns regarding quality of mental health services, with 48.8% of CW and 34% of RP indicating that they did not believe the quality of available mental health services was good.

Conclusions: Descriptive examination of the data indicated difficulty accessing mental health services by both CW and RP. RP perceived mental health services as slightly less available compared to CW. Many CW and RP expressed dissatisfaction with the quality of available services and rated mental health services as difficult to access. The finding that high percentages of CW are not utilizing available resources to access services indicates that educating CW on using these services may improve foster children's access to care.

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SUICIDAL IDEATIONS AND MAJOR DEPRESSIVE DISORDER IN TWO TEENAGERS PRESENTING FOR ROUTINE CARE IN A PEDIATRIC MOBILE CLINIC

A. Olteanu, M. Johns, D. Usner, R. Arnberger, E. Zimmerman *Tulane School of Medicine, New Orleans, LA.*

Case Report: The New Orleans Children's Health Project (NOCHP) is a pediatric program developed as a partnership between the Children's Health Fund and Tulane School of Medicine and operates out of two mobile units employing an enhanced medical home model. Our medical unit offers

pediatric primary care services and our second unit provides mental health services to children and their families. NOCHP provides services in four underserved communities in the Greater New Orleans area.

Depression in patients with and without co-morbidity is under recognized by pediatricians on average by 30% to 70% respectively. Early detection and treatment of major depression can reduce the occurrence of chronic depression in adulthood.

The American Academy of Pediatrics recommends yearly prevention visits for adolescents, during which high risk behaviors should be assessed. The Guidelines for Adolescent Preventive Services (GAPS) is a commonly used tool that screens for high-risk behaviors in adolescents. We would like to discuss two cases involving teenagers who were diagnosed with suicidal ideations during their first visit with NOCHP. These teenagers presented for immunizations and weight management respectively. The first patient, a 12-year-old female, presented for immunizations and a well-child visit. During this visit, the patient completed the GAPS questionnaire and admitted to having been suicidal for years. She was immediately referred to the mental health unit for a risk assessment. She was diagnosed with Major Depressive Disorder and initiated on antidepressant medication. She was later admitted to a psychiatric inpatient facility for further treatment.

The second patient, a 14-year-old male, presented for weight management. As part of the initial visit, the patient filled out the GAPS questionnaire, which revealed suicidal ideations. He immediately underwent a risk assessment on the mental health unit and was diagnosed with Major Depressive Disorder with psychotic features.

These two cases illustrate that routine screening by pediatricians for mental health issues and the integration of mental health services into primary care may prevent complications related to depression in vulnerable teenagers and ultimately save lives.

Adult Clinical Case

Joint Poster Session

5:00 PM

Thursday, February 25, 2010

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MALIGNANT HYPERTENSION MASQUERADING AS THROMBOTIC THROMBOCYTOPENIC PURPURA

MZ. Bawany, B. Saeed, A. Mutgi *University of Toledo Medical Center, Toledo, OH.*

Purpose of Study: Hypertension is common but with early detection and treatment of hypertension, it is rare to see malignant hypertension. We report a patient who presented with signs suggestive of TTP and severe hypertension which resolved with the treatment of hypertension.

Methods Used: A 34-year-old African American male presented to the emergency department (ED) having experienced nausea, vomiting and diarrhea for 2 days. He denied hematochezia, melena or sick contacts at home. He complained of blurry vision without photophobia, headache but mild chest discomfort in the ED. Past medical history was unremarkable. The patient did not have any significant family history. Smoking history was significant for a pack of cigarettes daily for seven years, drank alcohol occasionally. His blood pressure upon presentation was 201/151 mm Hg, pulse was 103 beats per minute, respirations were 20 per minute and temperature was 98.4 F. Physical exams were unremarkable and he had no focal neurological deficits.

Summary of Results: His labs were: Hb 12.6 g/dl, WBC 13.9 Platelets 67000, Na 136, K 3.4, BUN 24, Cr 2.56 and LDH 556. Chest x-ray showed cardiomegaly and a non-contrast computed tomography scan of the brain was negative for any stroke (hemorrhage). Peripheral smear was significant for the schistocytes suggesting ongoing hemolysis. Urinalysis was positive for 4+ proteins, a large amount of blood, 0 to 2 white blood cells/high power field (HPF) and 0 to 2 red blood cells / HPF. Renal ultrasound was unremarkable.

Patient was treated with labetalol drip initially and his blood pressure decreased to 138/86 and then IV medications were switched to an oral regimen and the platelets count and creatinine gradually returned to normal as the blood pressure came under control.

Conclusions: This case report highlights that malignant hypertension is rare and it's a medical emergency which can present with feature resembling wide variety of diseases (including TTP and HUS).

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DEATH SENTENCE REVERSED: AN UNCOMMON BENIGN TUMOR OF THE PANCREAS

P. Esiobu¹, D. Youssef¹, D. Freeman¹, RD. Smalligan² ¹East Tennessee State University, Johnson City, TN and ²Texas Tech Univ Health Sciences Center, Amarillo, TX.

Case Report: An 85yo man presented with recent onset intense intermittent epigastric pain. He denied reflux symptoms, fever, sweats, chills, melena and weight loss. PMH: osteoarthritis, cholecystectomy. MEDS: aspirin. P/S: no smoking, and no alcohol. Physical exam: normal except for epigastric tenderness. Labs: Hgb 13.8, normal electrolytes, amylase and LFTs. Abdominal CT: 5x5cm mass in the tail of the pancreas. CT guided biopsy was consistent with a microcystic serous cystadenoma. **DISCUSSION:** The discovery of a pancreatic mass is usually devastating news since 95% of pancreatic tumors are malignant adenocarcinoma. In spite of advising the family that these are sometimes benign, our patient and his family spent days in anxiety awaiting the biopsy results given such a high likelihood of a death sentence being delivered. In our case, and the final diagnosis was a lesion that typically follows a benign course and makes up about 1% of pancreatic tumors: serous microcystic cystadenomas. The average age at diagnosis of these tumors is 63 and they are more common in women than men (3:1). Vague abdominal pain and vomiting are common in 2/3 of patients, with the remainder of the tumors being found incidentally. Microcystic cystadenomas are usually found in the tail of the pancreas as in our case, but occasionally they are found in the head and may obstruct the biliary tract causing jaundice. If fine needle aspiration is not definitive, the mass must be entirely resected since mucinous cystadenomas are malignant. There have been case reports of serous cystadenomas turning malignant but this is the exception rather than the rule. Thus, the general management of this tumor is to monitor its growth and any related symptoms. The average size of a serous cystadenoma at the time of diagnosis is 6cm and they typically grow about 2cm per year, sometimes reaching 25cm in diameter. The chief indication for resection is impingement on surrounding organs causing pain or other symptoms. In our case, the definitive biopsy and lack of alarm symptoms allowed a sigh of relief for the patient, family and physicians, and the patient has done well for almost one year with serial CT scans.

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CAT IN THE CRADLE - A CASE OF PASTEURILLA AND PROSTHESIS

DM. Freeman¹, B. Guha¹, RD. Smalligan² ¹ETSU Quillen College of Medicine, Johnson City, TN and ²Texas Tech Univ Health Sc Center-Amarillo, Amarillo, TX.

Case Report: An 86yo woman with a history of CAD, AF, DM and left total knee arthroplasty (TKA) presented with weakness and shortness of breath. She was febrile, had rales, a L knee effusion and a WBC of 11,000 with 88% neutrophils. CXR showed infiltrates and ceftriaxone was started. During treatment knee became erythematous and warm. Blood cultures grew *Pasteurella multocida* x2, hence her knee was tapped showing 38,000 WBCs with 83% PMNs and negative Gram stain and culture. Additional history revealed recent scratches by one of the patient's cats. Orthopedic and ID consults concurred that the patient was too ill to withstand surgical removal of the infected joint, opting instead for conservative management. Ceftriaxone was increased to maximum doses and the patient was discharged several days later for long-term antibiotics via a PICC line.

Discussion: *P. multocida* is a small Gram-negative rod that is part of the normal flora of the respiratory and digestive tracts of domestic animals. The organism commonly causes cellulitis following a bite or scratch, however, serious systemic disease can occur including pneumonia, sepsis, endocarditis, meningitis, and osteoarticular infection. Only a few cases of TKA infection by *P. multocida* have been described over the past 20 years, as the most common pathogen in TKA infection is *Staphylococcus*. Our patient appears to have been infected via cat scratches which led to bacteremia, pneumonia and ultimately prosthesis involvement. The negative synovial culture was likely due to pre-treatment with 3 days of IV antibiotics. Typical treatment for TKA infection is two-stage revision: removal of the prosthesis with placement of a spacer followed by reimplantation after 6 wks of antibiotics. This approach achieves a 90% success rate. In patients with significant comorbidities who cannot tolerate the procedure, conservative treatment with long-term antibiotics and/or arthrodesis of *P. multocida* septic arthritis has had favorable outcomes, though rarely attaining cure. Biofilm formation on prostheses provides a haven for

bacteria in such cases since they are largely impenetrable to antibiotics. This case reminds physicians to carefully evaluate any prosthetic joint in the setting of bacteremia.

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MOYAMOYA

K. Gandla, LS. Engel *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: Moyamoya is a rare progressive cerebrovascular disorder that affects the blood supply by causing blockage to arteries mostly around the Circle of Willis. This disorder is primarily seen in children and occasionally in adults (aged 30 to 40 years). Manifestations of this disease include recurrent transient ischemic attacks or stroke accompanied by muscular weakness or paralysis affecting one side of body.

A 40-year-old Hispanic woman with a past medical history of type 2 diabetes mellitus, hypertension, and poor medical compliance presented to the emergency room with 4 day history of right sided weakness and slurring of speech. Vital signs on admission were unremarkable except for a blood pressure of 208/113. Physical examination was significant for dysarthria, loss of right nasolabial fold and right sided motor weakness. Cerebral arteriogram demonstrated stenosis of the cavernous segment of the right internal carotid artery and complete occlusion of the right middle cerebral artery with collateral circulation between lenticulostriate and mirabel vessels. Stenosis of the cavernous segment of left internal carotid artery with severe stenosis of left middle cerebral artery with retrograde collateral circulation between posterior communicating and middle cerebral arteries on both sides was also noted. The patient was admitted and managed medically to control her blood glucose and blood pressure. The patient was transferred to a rehabilitation facility with appointments for further evaluation for bypass surgery to correct the cerebrovascular stenosis.

Moyamoya disease is a rare vasculocclusive disorder which affects the intracerebral segments of the internal carotid arteries. The resultant collateral network of blood vessels resembles cigarette smoke (Moyamoya-Japanese) on neuroimaging. Moyamoya disease should be considered in a relatively young patient with stroke and these patients should be evaluated for patency of cerebral circulation. Timely diagnosis and intervention (bypass surgery) is required to prevent the morbidity and mortality associated with the strokes associated with progressive narrowing of the cerebral arteries.

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THE HIDDEN DIARRHEA CULPRIT: LYMPHOCYTIC COLITIS

U. Ghaffar¹, RD. Smalligan² ¹East Tennessee State Univ., Johnson City, TN and ²TTUHSC, Amarillo, TX.

Case Report: A 69yo man presented with 5 weeks of diarrhea, nausea and abdominal discomfort which began about when he started a weight loss medication. He denied bloody stools, fever or weight loss. Despite stopping the medicine and taking bismuth subsalicylate, symptoms persisted and hence GI was consulted and colonoscopy was recommended. PMH: HTN, osteoarthritis, sleep apnea and erectile dysfunction. Meds: aspirin, tidalil. PE: soft abdomen without organomegaly. Labs: CBC, CMP normal. Colonoscopy was normal colon but biopsy showed lymphocytic colitis. The patient received mesalamine and a prednisone taper with resolution of symptoms by 2 weeks.

Discussion: Chronic diarrhea is a common complaint seen by internists and GI specialists alike. Common etiologies are irritable bowel syndrome, medication or radiation side effects, inflammatory bowel disease or some infectious cause. Our patient illustrates an uncommon but treatable cause of chronic diarrhea: lymphocytic colitis (LC). LC is one of two types of microscopic colitis, the other being collagenous colitis (CC). The causes of both are unknown, and both are more prevalent in older adults, though they affect men and women equally. These conditions have been associated with celiac disease, diabetes, rheumatoid arthritis, thyroid disorders, pernicious anemia and scleroderma, suggesting a possible autoimmune etiology though familial forms have also been seen suggesting a genetic component. Medications associated with an increased risk of microscopic colitis include NSAIDs, lansoprazole, sertraline, ticlopidine, ranitidine and acarbose. Our patient was typical of how LC is diagnosed: a patient with chronic non-bloody diarrhea has an endoscopically normal colon, but biopsies show inflammation and increased CD4+ T cells in the colonic epithelium. Management involves a low fat diet and avoidance of alcohol, caffeine, spicy and lactose containing foods. More severe cases are

treated with antidiarrheals, cholestyramine, steroids, or other anti-inflammatory medications like mesalamine or sulfasalazine. This case reminds physicians to keep lymphocytic colitis in the differential diagnosis of chronic diarrhea and shows the importance of colonoscopy with biopsy when the etiology is not readily identifiable by usual historical, exam, and laboratory means.

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EXPLORING MYSTERIES OF PULMONARY ALVEOLAR PROTEINOSIS

S. Kanikireddy, P. Bass, S. Milligan, B. Statham *LSUHSC, Shreveport, LA.*

Case Report: Pulmonary alveolar proteinosis (PAP) is a rare idiopathic disease characterized by filling of alveoli with fluffy material that is periodic acid-Schiff (PAS) positive. The composition is similar to surfactant. Any disruption in surfactant catabolism can initiate immuno modulation in alveolar macrophages precipitating accumulation of phospholipids and other protein components of surfactant in alveoli. The triggering event can be an infection, malignancy, inhalation of mineral dusts or insecticides and alterations in immune function such as HIV. Recent studies suggested that functional deficiency of granulocyte-macrophage colony-stimulating factor (GM-CSF) plays a major role in the pathogenesis and detection of antibodies against GM-CSF can be an diagnostic tool.

Patient is 54 year old AAF presented with worsening dyspnea on exertion for the last two years. She stated that she is at a point where she could hardly walk 10 feet. On presentation she also complained of intermittent chest tightness which prevents her from taking deep breaths and occasional dry cough. Initial laboratory work including HIV, Hepatitis panel, ANCA pattern, Angiotensin Converting Enzyme, Anti nuclear antibodies, Myeloperoxidase, Proteinase levels were normal. Echocardiography was normal. Chest X-Ray showed ground-glass opacities in both lungs with basilar predominance. Ultrasound for DVT was negative. CT of the chest showed Bilateral diffuse ground glass opacity in a crazy paving representing an infection or any chronic lung disease. Biopsy was obtained by video assisted thoracoscopy. The pathology came back positive for pulmonary alveolar proteinosis and PAS stain was positive. The whole lung lavage with normal saline was done. Patient responded well to the treatment and she was also explained the need for repeated lavages if symptoms recur.

Management of PAP is based upon the progression and the degree of functional impairment. G-CSF administration is becoming a routine part of the treatment protocol but the ultimate goal is to clear the alveoli which can be achieved by whole lung lavage with normal saline. Lung transplantation is reserved for congenital PAP or for end stage fibrosis. Prognosis is generally good with many patients going into complete remission though some require repeated lavages and have a poor outcome.

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WHEN WARFARIN IS NOT ENOUGH

PR. Lopez¹, DW. Stewart², RD. Smalligan³ *¹East Tennessee State University, Quillen College of Medicine, Johnson City, TN; ²East Tennessee State University, Bill Gatton College of Pharmacy, Johnson City, TN and ³Texas Tech University Health Sciences Center, Amarillo, TX.*

Case Report: A 66yo woman with recurrent DVTs was admitted with slowly worsening swelling of the right leg. She had been carefully maintained on warfarin for years. Given the indolent nature of the swelling and a therapeutic INR, she was treated initially with diuretics and compression stockings for venous stasis dz. When the pain and swelling became intense an ultrasound showed a new thrombus in the femoral vein. PMH: Crohn's disease, short bowel syndrome, CAD, HTN, and GERD. No h/o recurrent abortions, cancer or other hypercoagulable conditions. Family hx: mother with Crohn's and recurrent DVTs. Physical exam: neg except 3+ right leg edema and a positive Homan's sign. Lab: INR 5, and a negative hypercoagulable workup. Review of the patient's outpatient lab data showed a therapeutic INR >75% of the time (checked by home health), with no major fluctuations. Due to new thromboses despite anticoagulation she had an inferior vena cava (IVC) filter placed and warfarin was continued.

Discussion: Patients with inflammatory bowel disease (IBD) are known to be at increased risk of thromboembolic disease, even more so than patients with other autoimmune diseases such as RA and lupus. Proposed mechanisms of action for this propensity in IBD patients include alterations in mucosal hemostasis due to increased procoagulant factors, or dysfunction of coagulation inhibitors. Inflammation has also been associated with an

elevation of proteins involved in hemostasis and inhibition of fibrinolytic factors though our patient's Crohn's disease was quiescent. As in other prothrombotic conditions (Factor V Leiden, protein C, S, and antithrombin III deficiencies, antiphospholipid syndrome, cancers, etc.) management requires lifelong anticoagulation therapy with an INR target of 2-3. Presumably for reasons listed above, some IBD patients continue to form clots despite the use of warfarin (reports of up to 13% of such patients), similar to what is seen in patients with Trousseau's syndrome. An IVC filter can be used to prevent pulmonary emboli as was done in our case and LMWH or factor X inhibitors have been used as well in such patients.

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UNSTABLE C-SPINE FRACTURE

A. Lyon, L. Moreno-Walton *LSU Health Sciences Center, New Orleans, LA.*

Case Report: A 52-year-old male presented by ambulance to the emergency department complaining of severe neck pain and abnormal sensation in his right arm after sustaining a fall. He reports that his neck extended forcefully as he was falling, causing the back of his head to strike the upper step, which subsequently forced his neck forward in flexion. He immediately had the onset of severe neck pain and "pins and needles" sensation in his right arm. He was able to move his legs but did not attempt to ambulate secondary to pain. Paramedics arrived, fully immobilized him and then transported him to our emergency department. At the time of admit, vital signs were unremarkable and there was no sign of external trauma but he did appear in pain. He had tenderness to palpation over the posterior midline region of C4 to C7. Strength in both upper and lower extremities was 5/5 but he did have significant pain on movement of his right upper extremity. The patient was maintained in cervical immobilization and CT of the spine revealed a left C5-C6 jumped facet and a right C5-C6 perched facet. There was also 6 mm of anterior subluxation of C5 on C6 but no evidence of spinal cord compression or injury; no fracture was seen.

Neurosurgery took the patient for open reduction via a posterior cervical laminectomy. They then fused him at C5-C6. Postoperatively, the patient's right arm paresthesias and pain persisted and he developed mild weakness in both upper extremities after surgery. He began physical therapy and rehabilitation during his stay and developed no other deficits.

The injury in this case was very significant and had the potential to be devastating. Suspicion of an injury was high, given that our patient had the combination of pre-existing degenerative disease, considerable mechanism, severe neck pain, and a reported abrupt neurologic deficit.

Our patient had a very uncommon injury, a unilateral jumped facet with a contralateral perched facet, which was considered unstable and treated as a bilateral facet dislocation. This type of injury results from extreme hyperflexion of the neck, which causes anterior subluxation of the vertebral bodies due to ligamentous disruption. a high prevalence of associated spinal cord injury.

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NEPHROLOGISTS, NEUROLOGISTS, AND NEUROSURGEONS...A COMPLEX CASE OF THE SHAKES!

SK. Narmala, C. Moll, LS. Engel *LSU Health Sciences Center, New Orleans, LA.*

Case Report: We present a case of a 48 year old African American man with end stage renal disease and uncontrolled hypertension who presented to the emergency room with acute onset of weakness and "twitching" of his left upper extremity for one day. The patient recently had a spontaneous dislocation of the left shoulder which was reduced in the ER 2 days prior to presentation and was believed to be the cause of his current complaints. Physical exam was significant for mild motor weakness in the affected extremity. Labs were significant for an elevated BUN/Creatinine (59mg/dL/14.3mg/dL). His last known dialysis was a two days prior to presentation. A cat scan of the head was suggestive of a subacute 1.2 cm subdural hematoma (SDH) with no mass effect.

Neurology was consulted and he was admitted for observation and routine hemodialysis. The following day, his mental status deteriorated, he became progressively agitated, and was intubated for airway protection. Repeat head imaging showed no interval changes in the SDH. An EEG showed seizure activity originating from an epileptiform focus in the high right convexity of the head consistent with the patient's known underlying hematoma.

The hematoma was evacuated by neurosurgery. The next day the patient was successfully weaned off of sedation and extubated, with normalization of his mental status within 2 days. Given the quick recovery following the evacuation of the SDH, it was believed that his seizures were due to the hematoma all along.

Cognitive impairment in dialysis patients can result from uremia, medications or from cerebro-vascular accidents, more specifically subdural hematomas (SDH). Subdural hematoma is a known complication in long term dialysis patients; the frequency has doubled in the past few years. SDH are categorized as acute (<72 hrs), sub-acute (3–20 days) or chronic (>3 wks) based on the duration. Seizures are much more commonly associated with acute SDH than subacute or chronic SDH. Surgical evacuation of hematoma along with anti-epileptic medications has provided good results.

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SUPERIOR MESENTERIC ARTERY SYNDROME (“WILKIE’S SYNDROME”) IN A PATIENT WITH HEREDITARY COPROPORPHYRIA: CASE REPORT AND LITERATURE REVIEW

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Purpose of Study: Superior mesenteric artery (SMA) syndrome is rare and characterized by compression of the distal duodenum between the aorta and SMA. We present the case of SMA syndrome in a man who was priorly diagnosed with hereditary coproporphyrria (HC), and reported cases of SMA syndrome were studied.

Methods Used: A 24 year-old male presented with chronic symptoms of bilious emesis and midepigastic/RUQ abdominal pain. Patient had cholecystectomy for RUQ abdominal pain in 2007. In 2008 he was diagnosed with HC (plasma coproporphyrin level elevated at 13 mcg/L) and weighed 162#. He was variably controlled on intermittent hematin therapy for the past year, and multiply hospitalized with multiple follow-up computed tomography (CT) studies. Patient now weighed 116# on admission. He was treated conservatively for a presumptive ‘porphyria exacerbation’ with intravenous rehydration, hematin and antibiotics. CT scan, MRI and upper gastrointestinal series with small bowel follow-through were performed. What was replicably noted was a markedly enlarged and dilated duodenum proximal to the C-loop (ligament of Treitz) and an exceedingly narrow caliber jejunum distal to an area of focal compression, corresponding to the origin of the SMA as it came off of the aorta. Also, articles containing key words “Wilkie’s or SMA syndrome” were reviewed.

Summary of Results: The diagnosis of SMA Syndrome was made. Over the course of this patient’s year-long 46# weight loss, progressive lessening (and now absence) of the mesenteric fat separating the aorta and superior mesenteric artery’s origin in this patient was able to be serially assessed, when comparison of the many CT studies which had been performed on this patient since his diagnosis one year ago were assimilated.

Literature review reveals risk factors including thin body habitus, anorexia, weight loss, trauma, anatomy and congenital anomalies, surgery and local pathology.

Conclusions: This is the first reported case known to the authors to be found in the medical literature of SMA syndrome in a patient with HC. Also, it is important for physician to be aware of the diagnosis of SMA syndrome in patient with recurrent abdominal pain and cachexia.

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STROKE: WHERE IS IT COMING FROM?

A. Nguyen, L.S. Engel *LSU Health Sciences Center, New Orleans, LA.*

Case Report: A 59-year-old woman with past medical history of hypertension, diabetes, peripheral vascular disease, and chronic kidney disease stage III presented to the hospital with complaints of left lower extremity weakness for 1 day. The patient was in her usual state of health until 1 day prior to presentation when she had an episode of stumbling. She later noticed that she could not move or control her left leg. The patient also admits to numbness starting in her left toes and extended through her entire leg as the day progressed. She denied any dysarthria, aphasia, dyslexia, chest pain, or shortness of breath. On physical exam, there was a slight weakness in her left lower extremity (4/5 motor). The only other finding of note was bilateral carotid bruits. On CT scan of the head, she was found to have an old right basal ganglia lacunar infarct; no

acute intracranial hemorrhages were visualized. MRI of the brain showed an acute lesion in the right periventricular white matter consistent with a microvascular infarct. MRA of the neck was very suspicious for bilateral carotid bifurcation/internal carotid artery stenosis which were confirmed by a carotid duplex ultrasound with doppler. A transthoracic 2D echocardiogram demonstrated a mobile vegetation attached to the anterior mitral valve leaflet chordae. That test was followed up with a transesophageal echocardiogram which showed a advanced atherosclerosis and a large pedunculated and partially mobile mass (1.9 × 0.8 cm) attached to the medial aspect of the mitral annulus in the left ventricle.

The diagnosis of stroke was not the issue for the patient presented here; the etiology was the clinical conundrum. This patient had several possible sources for stroke including vascular disease and a valvular vegetation. Determination of the etiology of stroke is important so that proper therapy can be initiated in order to reduce the likelihood of future events.

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DOCILE OR DANGEROUS? A CASE OF HERPES SIMPLEX TYPE 2 MENINGITIS

L. O’Neal *Vanderbilt University, Nashville, TN.*

Case Report: A 40 year old man presented to our emergency department with complaints of three months of intermittent fevers and headache. These symptoms occurred in conjunction with diffuse myalgias, though he denied weight loss and reported no sinus congestion since starting intranasal steroids two months earlier. On the day of presentation, he complained of headache, photophobia, mild nausea, and generalized malaise. His exam was significant for fever to 101.5°F and neck tenderness, though no specific neurologic deficits were observed. Additionally, he had no rash, heart murmur, or lymphadenopathy. Lumbar puncture demonstrated 41 nucleated cells with lymphocytic predominance, glucose 55, and protein 53. A diagnosis of aseptic meningitis was made. Initial blood cultures, India ink stain, cerebral spinal fluid fungal cultures, and HIV test were all negative. Later, PCR testing for herpes viruses showed a positive result for HSV-2. Treatment with intravenous acyclovir was initiated, and his fever resolved. He eventually provided history of outbreaks of genital herpes, though he denied the presence of lesions in the six months prior to his presentation to the hospital. Overall he did well, though did not return for follow-up after discharge.

This case represents a potential outcome in any of the estimated one million new cases of HSV-2 infection occurring each year. At the time of the initial infection, the virus assumes latency primarily in the sacral ganglia, though it has also been observed throughout the entire central nervous system axis. Later reactivation is poorly understood, however chronic HSV-2 infection is known to lead not only to recurrent vesicular genital eruptions but also to recurrent neurologic symptoms. For example, patients with HSV-2 can develop recurrent aseptic meningitis, radiculopathy, cranial neuropathies, or acute retinal necrosis. Recurrent headache may occur in up to 15% of patients with HSV-2 infection, and this may be the single most apparent symptom of recurrent aseptic meningitis in the immunocompetent adult. Often times these headaches are self-limited, and do not require treatment. However, anecdotal evidence suggests that antiviral therapy can improve neurologic symptoms, though indications for their use remain unclear.

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OPHTHALMIC ULTRASOUND GOES TO THE RETINA

LR. Peebles, L. Moren-Walton, LD. Mills *LSU Health Sciences Center, New Orleans, LA.*

Case Report: A 38 year old man without any significant past medical history presented to the emergency department approximately 24 hours following an altercation in which he sustained a direct blow to the right eye with bare knuckles. He complained of instantaneous near total vision loss in the right eye following the punch, retaining the ability to only see shadows and faint outlines of objects. He had no complaints at the left eye. The patient was found to be in no distress with normal vital signs. Gross physical examination revealed only a few small abrasions to the face. There were no gross abnormalities to the external right eye. Computed tomography of the face and orbits was negative for acute fractures and extraocular eye movements were intact. Visual acuity was 20/800 and 20/20 in the right and left eyes respectively. Intraocular pressures were 12 and 14 in the right and left eyes respectively. Fundoscopic examination was normal on the left. However,

the fundus was not readily visualized on the right due to changes in the vitreous. Dilation of the pupil by ophthalmology did not improve visualization of the fundus. Ophthalmic ultrasound of the right eye using a high-frequency linear probe yielded adequate visualization of the posterior globe that demonstrated retinal injury.

In the setting of acute loss of vision, intraocular pathology should always be considered and prompt identification of retinal injury and subsequent evaluation and intervention by an ophthalmologist pursued. The emergency department is typically the initial point of presentation for injuries of this type; therefore, ED physicians must maintain a high level of suspicion to guarantee the best care for their patients. Ultrasonography continues to grow as a useful adjunct in the ED and, in the case of this patient, allowed the treatment team to make a relatively quick diagnosis.

51 PROTEINS GONE WILD

D. Robledo, B. Barker, P. Thien *LSU Health Sciences Center, New Orleans, LA.*

Case Report: A 58 year old man with a history of alcohol abuse presented to an outlying emergency department with a 2-3 month history of bilateral leg swelling that started in his feet and progressed to his abdomen. He also developed diffuse pruritus 1 week prior to admission. The patient was initially admitted for an elevated troponin (0.08 ng/ml), but was subsequently found to have an alkaline phosphatase of 2000 U/L. The patient developed hemoptysis after admission to the outlying hospital and was transferred to the LSU Interim Hospital for further evaluation. The patient's initial work-up included a right upper quadrant U/S and hepatitis panel, both of which were non-diagnostic, and a GGT level that was elevated. A paracentesis was performed which demonstrated portal hypertension, but an MRCP was unremarkable. A liver biopsy was obtained, and the results, confirmed by Congo red stain, were consistent with amyloidosis. Once the biopsy results were known, the hematology/oncology service was consulted and quantitative immunoglobulin levels were checked. IgE and IgA levels were both elevated, suggesting that the diagnosis was primary amyloidosis. The patient was told of his poor prognosis with this diagnosis (average life expectancy of 3-4 months); he deferred chemotherapy and chose to be placed in hospice care.

AL (primary) amyloidosis is a clonal plasma cell proliferative disorder characterized by light chain deposits in the tissue that cause organ dysfunction. The clinical presentation of this disease depends on the organs affected. Some common presentations include: hepatomegaly with elevated liver enzymes, nephrotic syndrome, restrictive cardiomyopathy, and purpura in the periorbital region. Approximately 10% of amyloidosis patients will also present with multiple myeloma. For patients who are not candidates for hematopoietic cell transplantation, the standard treatment is a combination of melphalan and prednisone. Complete remission following such treatment is uncommon and the prognosis is 4 to 6 months depending on which organs are involved.

52 A SEVERE CASE OF PITIRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA

J. White¹, K. Singh¹, D. Levy¹, LB. Tran¹, AF. Patenaude¹, EJ. Soine^{1,2}, LT. Nesbitt², LS. Engel¹ *¹LSU-Health Sciences Center, New Orleans, LA and ²LSU Health Sciences Center, New Orleans, LA.*

Case Report: Pityriasis lichenoides et varioliformis acuta (PLEVA), also known as Mucha-Habermann disease, is an uncommon cutaneous disorder characterized by an acute, diffuse eruption of erythematous to purpuric macules and papules. The lesions often favor the trunk and progress through stages of central necrosis, crusting, and eventual varioliform scarring. PLEVA represents the acute variant of pityriasis lichenoides (PL). We present an unusual case of the ulceronecrotic variant of PLEVA.

A 32-year-old woman presented to the emergency department with a 3 week history of a generalized, desquamating eruption. The eruption consisted of numerous red-brown macules with central necrosis coalescing into large areas of ulceration, especially involving the flexural arms and medial thighs. The eruption covered most of her body surface area, sparing the palms, soles, axilla, intertriginous areas, and mucosa and had limited involvement on the face. She denied constitutional symptoms such as fever or malaise. The patient had been treated with topical steroids, permethrin cream, and oral steroids by outside physicians without significant improvement. Laboratory workup was essentially unrevealing including negative

ANA, p-anca, c-anca, RPR, and HIV. The patient was admitted and responded favorably to intravenous steroids, doxycycline and intramuscular methotrexate. The patient was transitioned to oral prednisone and continues to improve on weekly methotrexate and doxycycline.

Severe cases of PLEVA may be difficult to discern from Steven-Johnson syndrome, toxic epidermal necrolysis, and erythema multiforme. Our patient had sparing of mucosal membranes, absence of fever, and characteristic red-brown macules with central necrosis, pointing to the diagnosis of PLEVA. Her large patches of ulceration were more typical of the ulceronecrotic variant of PLEVA. Diagnosis is confirmed by histological assessment of the skin. Treatment successes have been described with topical steroids, ultraviolet light, tetracyclines, low dose methotrexate, and systemic steroids for the ulceronecrotic variant. Prognosis is generally good with a benign course, though malignant transformation has been described.

Allergy/Immunology/Rheumatology Joint Poster Session

5:00 PM
Thursday, February 25, 2010

53 USE OF IMMUNOMODULATORY HIGH-DOSE SUBCUTANEOUS IMMUNOGLOBULIN IN TREATMENT OF OPSOCLONUS MYOCLONUS SYNDROME

D. Alle, JM. El-Dahr *Tulane University Medical Center, New Orleans, LA.*

Case Report: Rationale: Opsoclonus Myoclonus Syndrome (OMS) is a rare, autoimmune condition resulting in abnormal eye movements, involuntary twitching of muscle groups, ataxia, irritability, and speech impairment. High dose intravenous immunoglobulin is part of the standard therapy in pediatric patients diagnosed with OMS. We report a 2-year old girl who was diagnosed with OMS, initiated on intravenous immunoglobulin, and successfully converted to a high-dose subcutaneous immunoglobulin regimen.

Methods: Case report of a 2-year old girl diagnosed with OMS who initially presented with neurologic symptoms of arm and leg tremors, and unsteady gait at 22 months.

Results: CSF studies, EEG, MRI of the brain and spine were normal. CT scan revealed no neuroblastoma. Blood chemistries and metabolic panels, including a carnitine panel, DNA ataxia panel, and lead test were normal. Initiated on corticosteroids (2 mg/kg daily) at age 22 months and intravenous immunoglobulin at 26 months (1 g/kg IV monthly for 9 months.) Had improvement in symptoms and successful weaning of steroids. However, severe headaches and vomiting were experienced after each intravenous dose despite pre-treatment. Converted to a high-dose subcutaneous immunoglobulin protocol (2200 mg/kg every 6 days) with continued improvement in gait and neurologic function with no further episodes of vomiting or headaches.

Conclusions: Current therapeutic guidelines for OMS recommend a trial of IVIg (1 g/kg of body weight monthly) should be implemented for 3-6 months with continued therapy every 3-4 weeks afterwards if successful. We suggest that a high-dose subcutaneous immunoglobulin protocol may be effective with fewer side effects in pediatric patients with OMS.

54 A CASE OF LUPUS-INDUCED PANCREATITIS

M. Borrisov, K. Schurman, L. Espinoza *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: A 24 year old women with a past medical history of Systemic Lupus Erythematosus (SLE) on chronic steroids, lupus nephritis, antiphospholipid Syndrome, anemia of chronic disease, and hypertension was admitted to the hospital with two weeks of progressively worsening, diffuse, burning abdominal pain associated with nausea, vomiting, and diarrhea. The patient denied any alcohol or drug use. The patient had a cholecystectomy one month prior to admission. At the time of admit, physical exam was significant for tachycardia and epigastric tenderness; bowel sounds were present. Laboratory values included a white blood cell count of $14.8 \times 10^3/\mu\text{L}$ with 20% bands, Amylase of 166 U/L, Lipase 746 U/L, Alkaline phosphatase 169 U/L, Total Bilirubin of 0.6 mg/dL, and Triglycerides of 109 mg/dL. Connective tissue workup confirmed active lupus with a positive ANA, C3 of 22 mg/dL, C4 of 7 mg/dL, and Anti-dsDNA of 1:1280. CT imaging of her abdomen showed

stranding and fluid surrounding the pancreas, suggestive of acute pancreatitis without signs of ductal dilation. The patient was placed on high dose methylprednisolone for three days, intravenous fluids, vancomycin and piperacillin-tazobactam. Hydroxychloroquine was continued, however mycophenolate mofetil was held during the hospital stay because it was thought to be contributing to her renal failure. The patient started tolerating oral nutrition, had improved abdominal pain, and normalization of her white blood cell count and serum chemistries through her hospital course.

Pancreatitis is an uncommon manifestation of SLE. Other etiologies of pancreatitis such as hypertriglyceridemia, alcoholism, gallstones, infection, trauma, and medications should be excluded before a diagnosis of SLE pancreatitis can be made. Patients with severe SLE who are on immunosuppressive therapy such as glucocorticoids are at increased risk of pancreatitis. The use of these immunosuppressive therapies may occasionally be the cause of pancreatitis in these patients. This particular patient was on chronic steroids for her SLE; however her physical exam and laboratory values improved on high dose steroids and medical management during the hospital stay which argues against steroid-induced pancreatitis.

55 BILATERAL ORCHITIS IN LUPUS/SCLERODERMA OVERLAP SYNDROME

ER. Boulis, V. Majithia *University of Mississippi, Jackson, MS.*

Case Report: Testicular involvement has previously been reported in only 3 cases of SLE and none in systemic sclerosis. We present an unusual case of orchitis in a patient with overlap connective tissue disease (CTD)- SLE and systemic sclerosis.

A 28-year-old African American male presented with a 3 day history of testicular and abdominal pain. He had a history of overlap CTD (SLE and systemic sclerosis). SLE features were polyarthritis, serositis, lymphopenia, positive ANA, anti-DsDNA and anti-Smith antibodies while systemic sclerosis features were sclerodactyly, diffuse skin thickening, severe raynaud's and positive anti-centromere antibodies. Prior to admission, he was on prednisone 5 mg daily, calcium channel blockers and aspirin. On exam, he was afebrile, had lower abdominal and bilateral scrotal tenderness with scrotal swelling. Laboratory tests showed lymphopenia, low complements, elevated ESR, CRP and anti-DsDNA antibodies. CBC, complete metabolic panel and urine analysis were normal. Blood and urine cultures, chlamydia and gonorrhea PCR, antiphospholipid antibody panel, lupus anticoagulant, hepatitis panel, ANCA and cryoglobulins were negative. Testicular MRI and ultrasound showed bilateral testicular wedge shaped areas of decreased enhancement and echogenicity, representing areas of infarction. No evidence of microaneurysms or testicular torsion. Patient refused to undergo a testicular biopsy. A diagnosis of bilateral orchitis and serositis was made. He was successfully treated with prednisone 1mg/kg/day and azathioprine. At 4 weeks follow up, his testicular and systemic symptoms completely resolved and laboratory values markedly improved.

Orchitis in CTD is usually secondary to medium vessel vasculitis, classically described in polyarteritis nodosa. SLE and systemic sclerosis cause small vessel vasculitis which is not typically associated with orchitis. In this patient, the testicular symptoms were likely caused by vasculitis related to his overlap syndrome. This also seemed to be a flare-up of SLE rather than systemic sclerosis due to low complements, elevated anti-DsDNA antibodies, lymphopenia, serositis and disproportionately high ESR compared to CRP. Our case highlights that although testicular involvement secondary to small vessel vasculitis in CTD is uncommon, it is still possible and should be evaluated.

56 WEGENER'S GRANULOMATOSIS: A RARE PEDIATRIC DIAGNOSIS

D. Edgeron, W. Wells, J. Bocchini *LSUHSC-Shreveport, Shreveport, LA.*

Case Report: This is a case of a 9 year old black female presenting with productive cough, subjective weight loss, and fatigue for three weeks. Three months prior to presentation, the patient had earache, nasal congestion and facial pain and was diagnosed with sinusitis and otitis media. Her symptoms did not improve with amoxicillin or azithromycin. Concomitantly, she had polydipsia and was diagnosed with a urinary tract infection. Her cough worsened at night along with dyspnea. Chest radiograph revealed right upper lobe infiltrate and she was empirically treated with ceftriaxone, without

resolution. CT of the sinuses revealed pansinusitis with mucosal thickening of the sphenoid sinus. CT of the thorax revealed a large infiltrate in the right lung, upper lobe. The patient was empirically treated with vancomycin and ceftazidime for complicated pneumonia, but later changed to clindamycin and piperacillin/tazobactam. Lack of resolution resulted in the wedge resection of her right lung. Histopathology revealed necrotizing granulomas and pneumonic changes with interstitial fibrosis. C-ANCA level was elevated. The patient's renal function declined and microscopic hematuria and proteinuria were noted. Renal ultrasound showed diffuse increased echogenicity of both kidneys, likely representing chronic renal disease. The patient's BUN and creatinine continued to rise, resulting in the need for hemodialysis. The patient's clinical findings, pathology, and laboratory results were consistent with Wegener's granulomatosis, a rarity in the pediatric population. She was treated with cyclophosphamide and plasmapheresis. Her dyspnea and cough resolved. Cyclophosphamide and plasmapheresis were stopped and low dose prednisone was started. Afterward, the patient's blood pressure increased and patient had three generalized seizures. MRI revealed changes in intracranial pressure. The seizures were due to elevated blood pressure and vasculitis in the brain. The patient received five more days of plasma exchange and cyclophosphamide. Blood pressure was controlled with nifedipine and hydrochlorothiazide. The patient's renal function slowly improved and hemodialysis was no longer required. She has been continued on prednisone for maintenance therapy.

57 POSTPARTUM PRESENTATION OF KIKUCHI SYNDROME COINCIDENT WITH THE ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS IN A WOMAN WITH RASH, FEVER, AND CERVICAL LYMPHADENOPATHY

EW. Hung, M. Bhattacharjee, WD. Ratnoff *University of Texas Health Science Center Medical School at Houston, Houston, TX.*

Case Report: A 36-year-old Hispanic woman presented with rash, fever, and cervical lymphadenopathy. One month earlier she had preterm labor. Streptococcal pharyngitis was treated with ampicillin. Postpartum she experienced daily fevers attributable to E. Coli bacteremia, and was treated with other antimicrobials. She had pleuritic chest pain, and noted a nodule in her right neck. Two weeks later she was admitted for fever, chest pain, and lymphadenopathy. Fine needle aspiration of a small supraclavicular node was reported as hypocellular. Normocytic anemia required transfusion with packed red cells. Hours after the transfusion, she developed facial swelling with a red, raised rash of the face, trunk, palms, and extremities. Facial swelling improved transiently, and symptoms were attributed to the blood transfusion. She returned with persistent fevers, rash, and lymphadenopathy. Rheumatology consultation was requested. Angioedema of the upper lip gradually resolved over a week. Leukopenia, lymphopenia, and anemia were present. The AST was 168; she had mild proteinuria. The antinuclear antibody was positive, titer 1:640, homogenous pattern. The dsDNA antibody was positive with a titer of 20,480. The RNP and SS-A were positive. Smith and SS-B antibodies were negative. Complement C3, C4, and CH50 levels were low, but C1q, C2, and C1 esterase inhibitor levels were not diminished. The lupus anticoagulant was abnormal; the beta-2 glycoprotein IgA antibody was elevated. Infectious etiologies were excluded. Chest CT showed axillary and mediastinal lymphadenopathy and serositis. Neck CT showed lymphadenopathy. Right chest skin biopsy showed interface dermatitis, interpreted as lupus. Flow cytometry of the marrow biopsy showed no aberrant populations. Excisional right cervical lymph node biopsy showed extensive necrosis surrounded by sheets of histiocytes. She responded to therapy with prednisone and hydroxychloroquine. Kikuchi syndrome can present during pregnancy. In this patient, the clinical and pathologic features were consistent with Kikuchi syndrome coincident with the onset of systemic lupus erythematosus. There are few previously reported cases.

58 CHRONIC URTICARIA AND ANGIOEDEMA: THE FORGOTTEN PARASITE

G. Karamchandani-Patel¹, L. Wall², P. Kumar¹ *¹LSUHSC, New Orleans, LA and ²LSUHSC, New Orleans, LA.*

Case Report: Chronic urticaria (CU) is often a vexing illness for physicians and patients since up to 90% of cases do not have an identifiable

cause. Parasitic infections are a frequent cause of CU worldwide, and are often overlooked when treating patients in industrialized nations. Here we report a case of a parasitic infection in a patient with travel to an endemic area:

A 26 yo F presented with a 2 year history of generalized urticarial lesions and periorbital angioedema, progressing in frequency and intensity over the last 6 months. Episodes occurred 3 times/week, and lasted less than 24 hours. Episodes were unrelated to ingestions or medications. Travel history included a trip to India in 2006, 6 months prior to onset of her symptoms, during which she had an acute episode of gastroenteritis. Serology revealed an elevated eosinophil count (518/ μ L) and an elevated total IgE (1376 kU/L). Specific IgE antibodies to *Ascaris* were obtained and were elevated at 9.29 kU/L. Based on these results, she was treated with a single dose of mebendazole. At 3 month follow-up, symptoms had completely resolved, with improvement in serology.

Ascariasis is one of the most common helminthic infections worldwide. In the US, it is the third most frequent helminth infection. Transmission occurs mainly by ingestion of food/water contaminated by fertilized ova. These ova found in the environment, can be ingested by humans. Once ingested, the ova hatch in the small intestine and release larvae, which can penetrate the intestinal wall and migrate via blood or lymph vessels. The majority of patients with infections with *Ascaris* are asymptomatic and clinical symptoms are usually seen in those with a high worm load. Our patient's symptoms were likely due to a hypersensitivity reaction caused by an immunologic response to the larvae and/or adult worms.

Treatment of choice is typically with benzimidazoles, which act against the adult worm, not the larvae, and therefore close follow up is recommended to ensure complete elimination of the adult worms.

CU associated with eosinophilia may be secondary to numerous causes. In the US, atopic diseases are the most common causes. Parasitic infections are increasingly being encountered in industrialized countries therefore emphasizing the need to always obtain a thorough history.

59 TREATMENT WITH ETANERCEPT IN TWO PATIENTS WITH SARCOIDOSIS

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Purpose of Study: Sarcoidosis is a multisystem disorder of unknown etiology that is characterized pathologically by the presence of non-caseating granulomas in involved organs. Recently, antagonists to tumor necrosis factor- α have been proposed as a novel treatment strategy for sarcoidosis.

Methods Used: We are reporting two cases of sarcoidosis that have been successfully treated with etanercept. The first case is that of an eleven year old Caucasian girl who had been diagnosed with parotid gland, hilar lymphadenopathy, and lung involvement secondary to sarcoidosis five years prior. She had worsening pulmonary disease in spite of aggressive treatment with multiple medications. The second case is that of a thirteen year old African American boy who has been diagnosed with uveitis several years prior. After successful treatment and remission of uveitis, he developed live threatening sarcoidosis involving the central nervous system and lungs.

Summary of Results: The girl had progression of disease on aggressive treatment and the boy had toxicity related to disease modifying antirheumatic agents. Both children had an excellent response to etanercept and have continued on that medication with no apparent toxicity.

Conclusions: Our review of the literature revealed only one other pediatric case of sarcoidosis treated with infliximab; but to our knowledge, there are no previous reports of successful treatment with etanercept of pediatric patients with sarcoidosis.

60 CARDIOVASCULAR RISK IN SPONDYLOARTHROPATHIES (SPA) AND RHEUMATOID ARTHRITIS (RA) ON LONGSTANDING TNF-BLOCKERS

TA. Khan¹, R. Cuchacovich¹, J. Hagan², N. Patel¹, LR. Espinoza¹ ¹LSUHSC, New Orleans, LA and ²LSUHSC, New Orleans, LA.

Purpose of Study: To determine the role of long-term treatment TNF blockade (>60 months) in altering the risk of metabolic comorbidities in 2 cohorts of patients SpA and RA.

Methods Used: 68 adults patients; 36/68 RA (52.9%), 19 /68 (27.9 %) Psoriatic Arthritis (PsA) and 13/68 (19.1 %) Ankylosing Spondylitis (AS). Mean age PsA 49.6 (11.0) , AS 51.9 (13.2) years; mean disease and treatment duration PsA 172.75 (171.93), AS 151.16 (110.07) months; therapy: PsA: 22% DMARDs, 16.7% Naïve, and 61.1% TNF Blockers; AS: DMARDs 16.7%, Naïve 41.7%, TNF Blockers 41.7% . RA mean age and disease duration 47.2 (11.3), 52.3 (16.6), 51.2 (13.3) years and 102 (90.4), 72.9 (67.3), 71.3 (87.1) months; 10/36 TNF antagonists, 13/36 Methotrexate, and 13/36 naïve to treatment. Systolic (SBP) and diastolic (DBP) blood pressure, body mass index (BMI) were assessed. A quantitative ELISA assay for IL-6, sIL-6 R, IFN- γ , TNF α , sTNF- R I/RII, Adiponectin was performed. Fasting glucose, lipid profile, CRP and ESR were concomitantly done. Two-way ANOVA with interaction was used to examine the association of treatment and diagnosis with response variables.

Summary of Results: SBP was significantly higher for PsA than RA (p = 0.013). AS naïve patients had significantly (p<0.001) higher IL-6 levels than all other treatment-disease combinations. PsA TNF Blockers had significantly higher mean TNF α (p = 0.011) than all other diagnosis-treatment groups. RA patients had significantly higher mean sTNF RI levels (p <0.001) and significantly lower mean sTNF RII (<0.001), IFN- γ (<0.001), and adiponectin (<0.006) levels than PsA and AS subjects.

Conclusions: Longstanding TNF blockade therapy was associated with significantly higher levels of TNF α and sTNF α R1, and lower levels of sTNF RII and adiponectin. These findings suggest that biologic therapy with TNF blockers may affect the course of the ATE process in RA and SpA.

61 THE ANALYSIS OF LIPOTEICHOIC ACID FROM AN LIPOPROTEIN DIACYLGLYCEROL TRANSFERASE GENE DEFICIENT PNEUMOCOCCUS

T. Kim¹, R. Burton², DM. Miller³, N. Moon² ¹University of Alabama at Birmingham, Birmingham, AL; ²University of Alabama at Birmingham, Birmingham, AL and ³University of Louisville, Louisville, KY.

Purpose of Study: 1) To study the effects of the lgt gene in LTA from *S. pneumoniae*, we looked at the mass-spectra of LTA from a wild-type strain and an lgt mutant strain.

2) To further investigate the bioactivity of purified LTA and culture supernatant from the WT and lgt mutant.

Methods Used: 1) Bacterial strains and generation of supernatants. *Streptococcus pneumoniae* (strain TIGR4) was obtained. A non-encapsulated pneumococcal strain (TIGR4JS) was provided. A non-encapsulated variant (HS0001) was produced from TIGR4. An lgt deletion mutant (HS2009) was then created from HS0001. To obtain culture supernatant, bacteria was cultured in chemically defined medium to mid-log phase, bacteria was then pelleted by centrifugation, and the supernatants were filter sterilized.

2) Purification of LTA. Pneumococcal LTA was prepared using an organic solvent extraction and HIC using Octyl Sepharose.

3) Mass spectrometry. LTA was analyzed with MALDI-TOF mass spectrometry. For alkali hydrolysis the LTA samples were incubated with 0.2M NaOH and then dialyzed overnight.

4) Bioassays. Mouse macrophage cell line RAW264.7 were incubated with stimulants for 18 hours to measure the amount of tumor necrosis factor- α in the culture supernatant using ELISA. Nitric Oxide generation was determined using Griess Test. Human whole blood was incubated with stimulants for 18 hours. The amount of Interleukin-8 (IL-8) in the culture supernatant was determined with a sandwich-type ELISA.

Summary of Results: -The mass spectra of LTA from a wild-type strain and lgt mutant strain are similar, at least after alkali hydrolysis.

-One explanation for the difference in the bio-activity could be the acyl chains.

-From our data, we can say that the WT strain induces a higher amount of cytokines (IL-8 and TNF- α) and creates a higher level of inflammatory response than the lgt mutant.

-Possibly, the presence of alanine in purified LTA creates a higher level of bio-potency.

Conclusions: The lgt gene doesn't largely affect the biosynthesis of LTA. However, the results indicate that the lgt mutant gene does in fact play a role in the bioactivity of LTA.

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ACUTE ALCOHOL INTOXICATION INHIBITS STEM CELL ANTIGEN-1 EXPRESSION IN GR1+ MYELOID LINEAGE COMMITTED PRECURSOR CELLS DURING BACTEREMIA

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¹LSUHSC, New Orleans, LA; ²LSUHSC, New Orleans, LA and ³LSUHSC, New Orleans, LA.

Purpose of Study: Alcohol abuse is a major risk factor for developing bacterial infections. During bacterial infection, hematopoietic precursor cells preferentially commit toward the granulocyte lineage. Our previous studies have shown that enhanced stem cell antigen-1 (Sca-1) expression by lineage negative hematopoietic precursor cells is a key component of the granulopoietic response to bacterial infection. Alcohol intoxication impairs this response. It is currently unknown whether alcohol affects the Sca-1 response in myeloid lineage committed (Gr1+) cells. This study investigated Sca-1 expression by Gr1+ cells during bacteremia and the effect of alcohol on this response.

Methods Used: Thirty minutes after intraperitoneal alcohol injection (5g ethanol/kg), bacteremia was initiated by intravenous injection of *E. coli* (1 E6 or 5 E7 CFU). Intravenous BrdU (1mg/mouse) was administered at the time of *E. coli* challenge. Animals were sacrificed 24hrs after infection and bone marrow cells were analyzed by flow cytometry. Colony forming unit (CFU) assays of Gr1lo cells were performed by culturing sorted cells for 6 days in Methocult 3534 media.

Summary of Results: In uninfected animals, a greater percentage of Gr1lo cells expressed Sca-1 and incorporated BrdU than Gr1hi cells. Bacteremia increased the percentage of both Gr1lo and Gr1hi cells expressing Sca-1. Increased Sca-1 expression was accompanied by enhanced BrdU incorporation and CFU activity in Gr1lo cells. Gr1loSca-1+ cell CFU activity increased following bacteremia. Additionally, Sca-1 was re-expressed by Gr1+Sca-1- cells when cultured 12hrs in vitro with LPS. Alcohol intoxication suppressed the Sca-1 response, BrdU incorporation, and CFU activity of Gr1lo cells and inhibited the re-expression of Sca-1 by Gr1+Sca-1- cells.

Conclusions: These data show that alcohol suppresses Sca-1 expression in cells committed to myeloid lineage development during bacteremia. Inhibition of the Sca-1 response in downstream myeloid cells may serve as a mechanism underlying alcohol induced suppression of granulopoiesis and thereby impair host defense against bacterial infection. Supported by NIH NRSA AA09803 and AA07577.

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WHAT DO YOU MEAN YOU CAN'T TAKE PLAVIX!?!?

C. Moll, O. Nimkevych, LS. Engel, S. Kamboy *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: Clopidogrel, a thienopyridine, is a selective, irreversible inhibitor of adenosine diphosphate-induced platelet aggregation. Combination therapy of clopidogrel with aspirin after bare-metal stent (BMS), drug-eluting stent (DES), and even percutaneous coronary intervention (PCI) is a class I recommendation. Premature discontinuation of clopidogrel has been strongly associated with stent thrombosis.

An 83 year-old man presented to the emergency department complaining of tightness in his chest after taking out the garbage. The tightness lasted for 12 hours, was non-radiating, unrelieved with rest, and was not associated with shortness of breath, diaphoresis, nausea, or vomiting. His past medical history was significant for coronary artery disease with recent BMS placement 2 months ago, hypertension, hyperlipidemia, and chronic kidney disease. On further evaluation it was noted that the patient had not been taking his clopidogrel secondarily to a rash that developed on his arms soon after the medication was started.

Admit vital signs were significant for hypertension. Initial labs were unremarkable and cardiac enzymes were negative for myocardial ischemia. His EKG showed nonspecific ST and T-wave changes and first degree AV block similar to his previous EKG findings. An adenosine stress test was normal. Having been ruled out for acute myocardial ischemia, the patient was transferred to the ICU for clopidogrel desensitization. The patient tolerated the therapy without any complications and was discharged on 75mg clopidogrel on hospital day 4.

Although clopidogrel is tolerated by most patients, discontinuation of this medication has been seen in 4% of patients due to allergic reactions. The most common reaction is a pruritic, macular erythematous confluent rash;

however, other reactions of note are blood dyscrasias and angioedema. Other thienopyridine alternatives are available but cross-reactivity and side effects limit their successful use. Given the increased risk of coronary stent thrombosis with discontinuation of clopidogrel, physicians need to be aware that there are safe and successful rapid oral desensitization procedures to treat clopidogrel hypersensitivity.

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OSTEOPOROSIS RISK ASSESSMENT IN VETERANS AFFAIRS RHEUMATOID ARTHRITIS [VARA] REGISTRY PATIENTS

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Purpose of Study: Osteoporosis is a disease of bone with microarchitectural abnormality resulting in fracture. Accepted risk factors for osteoporosis include age, race, gender, steroid use, and others. The aim of this study was to investigate the interaction of race, disease activity and steroid use in the development of osteoporosis in a male RA population.

Methods Used: A retrospective chart review of 91 VARA patients, followed in rheumatology clinic from 12/01/07 to 06/01/09, was done. We separated patients into the following categories for analysis: normal or low bone mass (T-score < -1.0), none or 5 year average prednisone use, no disease activity or active disease at the most recent visit using two different measures. Active disease was defined as disease activity score (DAS28 with ESR) >2.6 or Multidimensional Health Quality Questioner (MHAQ) >1.0. We analyzed the effect of these variables on the presence of osteoporosis in black and white males independently using a two-tailed t-test or Fisher's exact test as appropriate. We considered an alpha <0.05 as statistically significant.

Summary of Results: Among 91 RA patients, there were 70 Caucasians and 21 African Americans. There was no difference in DAS28, MHAQ and chronic prednisone use between the two races. More white men than black men had low bone mass, $p = 0.001$. Blacks had higher T-scores both with inactive disease ($+0.04 \pm 1.28$ vs. -1.3 ± 1.65 , $p = 0.01$) and active disease ($+0.7 \pm 1.38$ vs. -1.5 ± 1.24 , $p = 0.06$ (trend). Elevated, but not low, MHAQ was associated with a lower T-score in white males (0.3 ± 1.57 vs. -1.6 ± 1.35 , $p=0.01$). There was no difference in the number of whites compared to blacks who develop low bone mass with high DAS28, MHAQ or chronic prednisone use ($p = 0.08$, $p = 0.168$, $p = 0.172$).

Conclusions: Our results show that Caucasians with RA have lower T-scores than African Americans; this was associated with MHAQ. This data suggests that race is still a more important risk factor for the development of low bone mass than disease activity and steroid use in male patients with RA.

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THE SCHOOL NURSE'S PERCEPTION OF FOOD ALLERGY - A STATEWIDE SURVEY

JM. Pulcini, G. Marshall *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: Several national organizations including the American College of Allergy, Asthma and Immunology, the American Academy of Pediatrics, the National Association of School Nurses and the Mississippi Department of Education recommend emergency action plans direct therapy of allergic reactions in children. Our study goal was to investigate the current food allergy management plans in Mississippi public schools.

Methods Used: A twenty question investigator-developed food allergy survey, modeled after one utilized to study school nurses in South Carolina, was offered to all public school nurses in Mississippi.

Summary of Results: Ninety-six of 346 eligible school nurses participated for an overall response rate of 28%. Ninety-seven percent (93/96) of the participating school nurses had at least one food allergic student at their school (mean 10 ± 9 food allergic students per school). The most common food allergens reported were peanut (80% of respondent schools) cow's milk (72%), egg (55%), fish (55%) and shellfish (54%). Twenty-eight schools (30%) had all of their food allergic students on a food allergy action plan where as 27 (29%) had 0-10% of their known food allergic students on food allergy action plans. The students were more likely to have food allergy action plans if the school nurse received information on food allergies from parents or a physician, or if the student attended a school in an urban area. p value <0.05, See Table 1.

Conclusions: Although multiple national and state organizations recommend food allergy action plans for food allergic students, our study highlights their inconsistent use in the state of Mississippi. Further research is indicated to investigate the causes for disparity between schools that do and do not adhere to the recommended school food allergy guidelines.

TABLE 1: Adherence to Food Allergy Action Plans in Mississippi Schools

	Percent of students with food allergy action plans	95% Confidence interval	p value (t-test)
Information from parents	61%	52-70%	p=.018*
No Information from parents	35%	14-56%	
Information from physicians	63%	53-73%	p=.022*
No information from physicians	42%	27-58%	
Urban area#	74%	62-85%	p=.002*
Non-urban area	46%	35-57%	

*p value <0.05 #Urban area defined as school in country with a city >25,000 inhabitants.

66 USING ELECTRONIC HEALTH RECORD AS A TOOL TO ASSESS ADHERENCE TO CLINICAL PRACTICE PARAMETERS FOR ALLERGIC RHINITIS

MW. Shepherd, JB. Wallis Louisiana State University Health Sciences Center, New Orleans, LA.

Purpose of Study: Intranasal corticosteroids are the most effective therapy for allergic rhinitis according to the Joint Task Force on Practice Parameters in Allergy, Asthma, and Immunology. The federally mandated electronic health record (EHR) is a useful tool to assess adherence to clinical practice guidelines. We used analysis of the EHR to evaluate how often a primary care clinic prescribes intranasal corticosteroids in patients with allergic rhinitis compared to an allergy clinic as well as the prevalence of nasal steroid use in adult versus pediatric patients.

Methods Used: Using the Allscripts EHR Analytics program, we pulled 556 patients with a diagnosis of Allergic Rhinitis (ICD-9 codes 477.x) from the LSU MedPeds clinic and LSU Allergy clinic who both use the Allscripts Enterprise EHR for patient visits. We then identified patients who were prescribed a nasal steroid. We placed these lists in Excel 2007 and used pivots tables to analyze the data and create charts. Chi square tests were used to evaluate statistical significance ($\alpha=0.05$) in SASv9.13.

Summary of Results: The Allergy versus MedPeds clinic difference in use of nasal steroids was 62.2% versus 47.8% which was statistically significant ($p=0.06$). The difference in prescription rates between the pediatric and adult populations in the MedPeds clinic was not statistically significant ($p=0.14$).

Conclusions: We found that within the primary care clinic, intranasal corticosteroids are prescribed less often for allergic rhinitis than in an allergy clinic. We hypothesize that dissemination of these findings to practicing primary care physicians might help them to better follow established guidelines of patient care for allergic rhinitis patients.

Cardiovascular
Joint Poster Session
5:00 PM
Thursday, February 25, 2010

67 ANOMALOUS ORIGIN OF THE RIGHT CORONARY ARTERY FROM THE LEFT CORONARY ARTERY IN A MAN WITH MITRAL STENOSIS

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Case Report: A single coronary arterial ostium is a rare congenital anomaly with an incidence of 0.024% in angiographic series. We describe a case of anomalous origin of the right coronary artery (RCA) from the left circumflex artery (LCX).

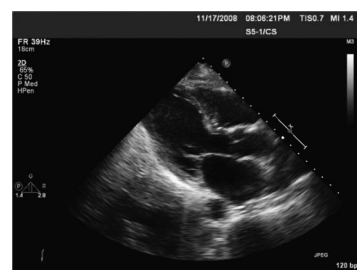
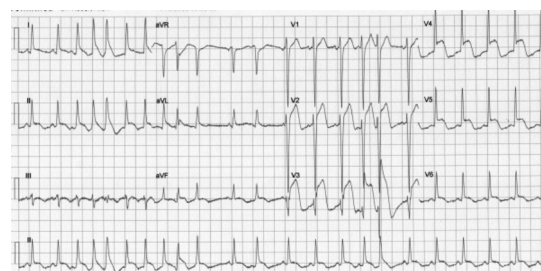
A 49 year-old man presented with shortness of breath on exertion and a grade 3/6 mid-diastolic murmur at the cardiac apex. Echocardiogram revealed severe mitral stenosis with a mean gradient 10mm of Hg and a valve area of 1cm². Coronary arteriography showed a large RCA with an uncertain course originating from the LCX, absent coronary ostium in the right sinus of Valsalva and an obstructive lesion in the left anterior descending coronary artery. Coronary computed tomographic angiography (CCTA) revealed the RCA originating from the proximal LCX and passing posterior to the aorta and anterior to the left atrium to reach the atrioventricular groove on the right.

A coronary artery with an anomalous origin can cause myocardial ischemia if it arises at an extremely acute angle from the aorta and thus has a slit-like ostium, if it is compressed between the aorta and the pulmonary trunk, or if it develops atherosclerotic narrowing. CCTA is useful in the assessment of the 3-dimensional relationship between the coronary arteries and the great vessels, which can be difficult to define by coronary arteriography alone.

68 STRESS (TAKOTSUBO) CARDIOMYOPATHY AND THYROTOXICOSIS

S. Kalra¹, R. Brenya¹, MA. Madani², RD. Smalligan³ ¹ETSU, Johnson City, TN; ²ETSU, Johnson city, TN and ³TTUHSC, Amarillo, TX.

Case Report: A 64yo woman presented with chest pain and shortness of breath two days after a car accident. PMH: hypertension. PE: normal except for sternal tenderness. Labs: troponin 1.99 (<0.5=nl), TSH <0.001, and elevated free T3, T4. CT showed no aortic dissection and the EKG had new anterior ST elevation. Left heart cath showed normal coronaries. Echocardiogram showed apical ballooning and an EF of 30%. The patient was managed with lisinopril, metoprolol and methimazole and the EF improved to normal within few weeks. **DISCUSSION:** Takotsubo cardiomyopathy is typically seen in elderly women with a recent stressful event that present with chest pain and EKG changes but normal coronaries. Echo reveals apical ballooning which is transient. Most agree that excess catecholamines play a role in this condition. Various theories exist regarding how thyroid hormones enhance myocardial sensitivity. We hypothesize that the combination of hyperthyroidism plus excess catecholamines from the crash was responsible for our patient's Takotsubo cardiomyopathy. Further research is needed regarding adrenergic receptor biology and the effect of thyroid hormones on the system.



69 MERITS AND FLAWS OF ANTICOAGULANTS USE IN THE SETTING OF CERVICAL ARTERY DISSECTION

R. Mohammed¹, A. Sumner² ¹LSU Health Sciences Center, New Orleans, LA and ²LSU Health Sciences Center, New Orleans, LA.

Case Report: Cervical artery dissection is increasingly recognized as a cause of stroke, particularly in younger people, with another peak incidence in the 50 year-old age group. Although neck trauma commonly precedes cervical artery dissection, there are several genetically inherited connective tissue disorders associated that increase the risk of it.

A 50 year old man with a history of hypertension, hyperlipidemia tobacco abuse, presented with slurred speech and left sided weakness affecting strength, balance and his ability to ambulate. There were no associated visual, hearing, or sensory deficits. Initial vitals showed a moderately elevated blood pressure, and physical examination was remarkable for a left arm intention tremor, dysmetria, and disidiadochokinesia as well as left leg dysmetria and an unstable tandem gait. Imaging studies demonstrated an ischemic stroke in the left posterior inferior cerebellar artery territory and a left basilar artery dissection. The patient was started on an aspirin, warfarin, simvastatin and hydrochlorothiazide. The patient's symptoms improved and he was discharged 4 days later.

A few days after discharge patient was brought to different hospital by EMS with complaints of drowsiness, headache and severe imbalance, which started 5 hours prior. Physical examination showed mild right side hemihypesthesia to pain, severe dysmetria in left leg and left arm and an intention tremor in the left arm. The patient's INR was 2.3. Imaging studies showed a massive hemorrhage in left cerebellar hemisphere.

Cervical artery dissection is often treated with anticoagulants to prevent ischemic stroke. The incidence of intracranial bleeding complications following anticoagulation treatment is 0.6% versus none following antiplatelet treatment. A systematic review showed no evidence of a therapeutic benefit favoring either antiplatelet or anticoagulant treatment in preventing Stroke, TIA or death in cervical artery dissection. The risk-benefit ratio of anticoagulation versus antiplatelet therapy remains unclear.

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ACUTE RIGHT VENTRICLE AND RIGHT ATRIUM COLLAPSE WITH NEWLY DIAGNOSED SYSTEMIC LUPUS ERYTHEMATOSIS

H. Grewal, LS. Engel *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: Cardiac involvement is a common finding with Systemic Lupus Erythematosus (SLE). Cardiac complications include pericarditis (most commonly), pericardial effusion, and myocarditis. Patients can develop pericardial effusions over time; however, they occur more frequently during an acute lupus exacerbation.

A 43 year-old woman with a history of bronchitis presented to the emergency department complaining of weight loss, rash, generalized fatigue and loss of hair for 3 months. At admit, abnormal vitals included blood pressure 97/57 and pulse rate of 112/min. Respiratory, Cardiovascular, abdominal and neurologic examinations were unremarkable. Skin examination revealed dry scaly rash on arms and hypopigmentation on frontal aspect of face. Lab work was consistent with a new diagnosis of SLE; treatment with hydroxychloroquine and prednisone was started. Transthoracic echocardiogram showed a small pericardial effusion. The patient returned 2 weeks later to the emergency department with acute onset shortness of breath. At that time repeat echocardiogram and CT of chest demonstrated a moderate size pericardial effusion with both right ventricular diastolic collapse and right atrial systolic collapse; there were no clinic signs of cardiac tamponade.

Pericardial effusions are seen in patients suffering from SLE and may be the initial presentation leading to a diagnosis of SLE. However in this case, the patient had a small pericardial effusion 3 weeks prior and then presents with acute shortness of breath secondary to a development of a moderate size pericardial effusion. Although the patient presented here remained stable, in many cases a pericardiocentesis may be needed. Currently no guidelines exist as to whether a therapeutic window should be done in these patients routinely secondary to their risk of developing a pericardial effusion or how often to screen with an echocardiogram. Further studies are needed to develop guidelines for screening and preemptive treatment of pericardial effusions in patients with severe disseminated SLE.

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HEART FAILURE AND ATRIAL FIBRILLATION

F. Musa, A. Shahzad, LS. Engel *LSU-Health Science Center, New Orleans, LA.*

Case Report: A 52 year old man with a past medical history of hypertension, heart failure, atrial fibrillation, and polysubstance abuse presented to the emergency department with worsening dyspnea for 4 days after consuming large quantities of alcohol and cocaine and running out of his medications. The Patient denied having any palpitations, chest pain, diaphoresis, dizziness, nausea or vomiting. Serum chemistries revealed a B-type natriuretic peptide concentration that was elevated greater than his baseline. His ECG was consistent with atrial fibrillation with rapid ventricular response. Chest- x ray revealed interstitial pulmonary edema. A transthoracic echocardiogram demonstrated moderate mitral and tricuspid regurgitation and severely decreased left ventricular systolic function with an ejection fraction of 20%. The patient was diagnosed with a heart failure exacerbation with superimposed atrial fibrillation and rapid ventricular response. He was treated with lasix, oxygen, low dose angiotensin-converting enzyme inhibitor (ACE), spironolactone, diltiazem drip and full dose anticoagulation. A beta blocker was added at discharge and patient was to follow up in clinic for AICD placement evaluation.

Atrial arrhythmias are common in patients with heart failure and cardiomyopathy. Among 382 individuals in a Framingham Study who had both heart failure and atrial fibrillation, 38% had atrial fibrillation first, 41% had heart failure first, and 21% had both diagnosed on the same day. Acute heart failure can precipitate atrial fibrillation due to the increase in left atrial pressure and wall stress. Conversely, atrial fibrillation can cause acute heart failure particularly if the ventricular response is rapid. Treatment options for atrial fibrillation with rapid ventricular response in the presence of decompensated heart failure involve rate or rhythm control. Therapy for acute heart failure may include sodium restriction, ACE inhibitor, β -blockers, diuretics, aldosterone antagonist, and digoxin. AICD placement after anticoagulation is considered for patients with an ejection fraction less than 35%. Combined treatment of atrial fibrillation and heart failure is essential for improved patient outcome.

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A REVERSIBLE CAUSE OF TACHYCARDIA-INDUCED DILATED CARDIOMYOPATHY

SS. Zaidi, AU. Shahbaz, KT. Weber *University of Tennessee Health Science Center, Memphis, TN.*

Case Report: Purpose: Thyrotoxicosis is a rare but important cause of reversible cardiomyopathy. To illustrate this rare but important consequence of hyperthyroidism, we report a patient with newly diagnosed hyperthyroidism due to Graves' disease and atrial fibrillation (AF), who presented with tachycardia-induced dilated cardiomyopathy leading to decompensated biventricular failure, which was reversed after achieving a euthyroid state and sinus rhythm.

Case Report: A 54-y/o African-American woman with no significant past medical history presented with a one-month history of palpitations and progressive dyspnea. Review of systems was positive for orthopnea, paroxysmal nocturnal dyspnea, fatigue, diarrhea and heat intolerance. Physical exam revealed an irregularly irregular pulse, BP 100/60 mmHg, respiratory rate of 18 breaths/min, and elevated jugular venous pressure. Patient had thyrotoxic ophthalmologic features and diffuse enlargement of the thyroid gland. Her apical impulse was displaced leftward and holosystolic murmurs of mitral and tricuspid regurgitation were present at the apex and along the left sternal border, respectively. Bibasilar crackles were heard and bilateral lower extremity edema was present. Electrocardiogram revealed atrial fibrillation with a rapid ventricular rate. Thyroid function studies: T_3 6.8 ng/mL, T_4 15.4 μ g/dL, TSH <0.02 μ U/mL. A dilated cardiomyopathy with four-chamber dilatation and ejection fraction (EF) of 30% was found by echocardiography. Standard treatment for congestive heart failure (CHF), together with a beta blocker and carbimazole, were initiated with clinical improvement. Radioactive iodine ablation of her thyroid gland provided a normalization of thyroid function tests. After achieving a euthyroid state, she had a complete recovery of her signs and symptoms of heart failure, including resolution of radiographic cardiomegaly, improvement in EF to 41%, and conversion to sinus rhythm.

Conclusion: Hyperthyroidism should be considered in all patients with new onset CHF associated with persistent sinus tachycardia or atrial fibrillation. Thyrotoxicosis is an uncommon but reversible cause of CHF and tachycardia-induced dilated cardiomyopathy.

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RARE CARDIAC ANOMALIES AND A UNIQUE COMBINATION

I. Hameed, VC. Guerra, M. Cassidy *Tulane University Heart & Vascular Institute, New Orleans, LA.*

Case Report: Background: Congenital malformations of the right atrium are rare and affect mainly a young age group. Very few cases are described in association with WPW syndrome in adults presenting as a narrow complex tachycardia. We are describing a unique case report of cardiac anomalies associated with a right atrial diverticulum presenting as a wide complex tachycardia.

Case Report: A twenty nine year old Hispanic female was brought to the ER by her friend with sudden onset of palpitations, chest pain and generalized weakness. She was found to be obtunded and hypotensive in the ER. The initial EKG showed a wide complex tachycardia with a rate of 260 bpm. She was successfully electrically cardioverted and placed on IV amiodarone. Subsequent EKGs showed WPW with a right-sided accessory pathway. Transthoracic echocardiography showed a cavity in her right ventricle, arising in the right atrium, bridging the AV groove and lying on the lateral wall of the right ventricle. The wall of the diverticulum seemed to be muscular and contracted with systole. The distal part of the right ventricular free wall appeared thinned and hypokinetic without aneurysms. Her subsequent workup, including TEE and CTA, confirmed a right atrial diverticulum but also showed anomalous origin of the right coronary artery from the left coronary sinus with an inter-arterial course. An EP study identified an accessory bypass tract inside the right atrial diverticulum which conducted well in both antegrade and retrograde directions. Because of its location on the ridge of the diverticulum we were unable to ablate the accessory pathway and the patient was referred to CT surgery for surgical ablation.

Discussion: Right atrial diverticulum (RAD) with an accessory pathway and the anomalous origin of the RCA from the left coronary sinus (ARCAOLS) are rare anomalies. To our knowledge these anomalies have never been reported in the same patient. These anomalies have been described separately in the literature with varied presentations secondary to palpitations, chest pain, SOB, myocardial infarction or sudden cardiac death. Therefore, surgical treatment with or without ablation of the accessory pathway should be considered in high risk patient.

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ACQUIRED GERBODE DEFECT DUE TO SEPTAL MYOMECTOMY AND MITRAL VALVE REPLACEMENT

I. Rajapreyar¹, F. Wilkoff¹, F. Helmcke² *¹Tulane heart and Vascular Institute, New Orleans, LA and ²LSU Health Sciences Center, New Orleans, LA.*

Case Report: Introduction: We shall describe a rare case of a Gerbode ventricular septal defect which was an iatrogenic complication of septal myomectomy and mitral valve replacement which caused right atrial enlargement and dyspnea.

Case: Patient was a 45 year old male with no past medical history underwent septal myomectomy and mitral valve replacement after a diagnosis of hypertrophic cardiomyopathy. In follow-up, the patient reported initial symptom-free recovery, complicated by a gradual and progressive onset of dyspnea on exertion. Transthoracic echocardiography revealed a normally functioning metallic mitral valve prosthesis and right atrial enlargement. Transesophageal echocardiography showed a defect in the membranous ventricular septum which acted as a shunt between the left ventricle and the right atrium, causing right atrial enlargement.

Discussion: Gerbode et al described the clinical significance of the syndrome of left ventriculo-atrial shunt in five pediatric patients and the defect accounts for less than 1% of congenital heart disease. Iatrogenic Gerbode defect can occur infrequently with infective endocarditis, trauma, aortic valve replacement or mitral valve replacement. The membranous septum is divided into atrioventricular and interventricular component by the septal leaflet of the tricuspid valve. The most common location of the defect is infravalvular, which is in the interventricular portion of the membranous septum. Our patient had the supraventricular defect which is in the atrioventricular portion of the membranous septum.

Conclusion: Increasing incidence of both percutaneous and open cardiac procedures makes this complication an increasingly relevant consideration in the differential diagnosis of patient with dyspnea and history of cardiac procedures.

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FIRST EPISODE OF ATRIOVENTRICULAR RECIPROCATING TACHYCARDIA

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Case Report: A 42-year-old man with diabetes mellitus, systemic arterial hypertension, dyslipidemia, tobacco use, and a myocardial infarct 10 years earlier had no history of arrhythmia. He underwent coronary arteriography because of exertional dyspnea. Results showed 3-vessel disease suitable for coronary artery bypass (CAB).

Ten hours postoperatively he developed a regular wide-QRS tachycardia at a rate of 208 beats/minute. With IV amiodarone, sinus rhythm returned. Because of ST-segment shifts suggesting inferoposterior injury on the 1st postop ECG 8 hours earlier and a higher than usual peak postop troponin I (11.84 ng/ml; reference < 0.09), the initial diagnosis was ventricular tachycardia. However, a left bundle branch block (LBBB) pattern with the nadir of the S wave less than 0.07 seconds from the onset of the QRS is typical of aberrant conduction and unlike ventricular ectopy. Aside from a brief episode of atrial fibrillation, the patient did well and went home on the 4th postoperative day. Two days later, however, he had 5 episodes of an identical wide-QRS tachycardia with rates ~ 190 beats/min; with each, sinus rhythm returned after IV adenosine. After amiodarone, runs of tachycardia were briefer; the rate was slower; and rate-related LBBB was seen less frequently.

Both with and without rate-related LBBB the ECGs indicate orthodromic atrioventricular reciprocating tachycardia utilizing a bypass tract. The R-P interval is less than the P-R, but the P wave is distinctly separated from the preceding QRS. A longer R-P interval with LBBB than with normal intraventricular conduction indicates a left-sided accessory pathway, and inverted P waves in leads II, III, and aVF are typical of a posteroseptal pathway. Ventricular preexcitation with a short P-R interval and a wide QRS complex with a delta wave were never seen during sinus rhythm or tachycardia in this patient. Thus, the accessory pathway only conducts retrogradely and is termed a concealed pathway. An electrophysiologic study revealed a posteroseptal accessory pathway, which was ablated.

Hundreds of patients with accessory pathways have undergone CAB operations. We are unaware of any patients whose first recognized arrhythmia utilizing the accessory pathway was in the first few postoperative hours.

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ENDOCARDITIS- THE COMPLETE SPECTRUM

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Case Report: Infective endocarditis (IE) is most frequently associated with *Staphylococcus aureus* or *Streptococcus viridans* infection. Risk Factors include intravenous drug use, valvular disease, HIV, prior endocarditis, and diabetes mellitus. Although prolonged antimicrobial therapy is the cornerstone treatment, a 30% risk of mortality remains.

A 34-year-old woman with a history of hepatitis C, hypertension, polysubstance abuse, diabetes mellitus, *Streptococcus viridans* endocarditis (aortic valve replaced in 2008), presented to the emergency department with syncopal episodes and diarrhea. At admit, vitals were temperature 101.3°F, and blood pressure 96/73. The patient was irritable and had a grade 4/6 holosystolic murmur at the left sternal border. Laboratory data demonstrated leukocytosis with a 14% bandemia, thrombocytopenia (platelet count 98,000/μl) and renal insufficiency (Creatinine 1.91mg/dl). Urine toxicology was positive for opiates and benzodiazepines. A transesophageal echocardiogram showed a dilatation of aortic root (58mm) with small vegetation. Blood cultures grew *Staphylococcus aureus* resistant to oxacillin (MRSA). The patient was treated

with vancomycin and rifampin; gentamicin was held secondary to renal insufficiency. Aggressive fluid therapy was initiated since the creatine increased to 3.5 mg/dL. Overnight, the patient complained of chest pain and EKG showed 2nd degree type I AV block alternating with first degree heart block with ST depressions in V1-V3. Cardiac enzymes were elevated (Troponin 17.8 ng/mL). The patient was transferred to the MICU and cardiothoracic surgery evaluated the patient but felt she was a poor candidate for surgical intervention. Despite aggressive medical management, the patient died of a non-ST segment myocardial infarction (NSTEMI).

We believe one of the main reasons for NSTEMI in this patient was coronary artery obstruction caused by external compression by a perivalvular abscess. There have been case reports of an aortic root abscess causing a dramatic elevation of the troponins. Surgery remains the mainstay treatment for perivalvular abscess. This case is unique because it shows the complete spectrum of endocarditis starting from small vegetation/abscess, and finally progressing to a myocardial infarction.

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IONIZED HYPOCALCEMIA WITH CALCIUM TRANSLLOCATION TO HEART AND SKELETAL MUSCLE: ACUTE STRESSOR RESPONSE TO ISOPROTERENOL

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Purpose of Study: Plasma ionized hypocalcemia occurs in patients having acute traumatic injury, the extent to which is reflective of the degree of injury and a determinant of prognosis. The fall in ionized $[Ca^{2+}]_o$ that accompanies acute stress may be related to catecholamine-mediated translocation of circulating Ca^{2+} to systemic tissues, and where intracellular Ca^{2+} overloading induces oxidative stress and contributes to tissue injury. Herein, we hypothesized the acute stressor state associated with isoproterenol administration, a synthetic catecholamine, would lead to ionized hypocalcemia and an increase in cardiac and skeletal muscle Ca^{2+} content.

Methods Used: Eight-week-old male Sprague-Dawley rats received subcutaneous isoproterenol (Isop, 1 mg/kg). At 8 and 24 h and 7 days after Isop treatment, plasma ionized $[Ca^{2+}]_o$ was monitored by ion-selective electrode, together with left ventricular and skeletal muscle (rectus femoris) tissue Ca^{2+} determined by atomic absorption spectroscopy. Untreated, unoperated rats served as controls.

Summary of Results: As compared to controls (1.19±0.01 mmol/L), plasma ionized hypocalcemia $[Ca^{2+}]_o$ ($p<0.05$) appeared at 8 h (1.08±0.01) and was resolved at 24 h (1.19±0.02) and 7 days (1.24±0.01). Compared to controls (5.1±0.2 nEq/mg), a marked ($p<0.05$) rise in myocardial Ca^{2+} was seen at 8 h (9.7±0.6), but which returned toward control levels at 24 h (6.4±0.8) and was normalized at 7 days (4.6±0.2). In skeletal muscle and compared to controls (3.3±0.1 nEq/mg), an excessive ($p<0.05$) accumulation of intracellular Ca^{2+} was found at 8 h (5.6±0.2) and 24 h (9.9±0.6), which returned to near control levels at 7 days (4.4±0.3).

Conclusions: The acute stressor state induced by a catecholamine is accompanied by early ionized hypocalcemia in association with an accumulation of Ca^{2+} in both myocardium and skeletal muscle, which fully resolves by 7 days. The plasma ionized hypocalcemia that accompanies the acute stressor state with isoproterenol includes its translocation to the heart and skeletal muscle. Intracellular Ca^{2+} overloading, in turn, can be responsible for the induction of oxidative stress and tissue injury.

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HYPOZINCEMIA AND ALTERATIONS IN TISSUE ZINC DURING THE ACUTE STRESSOR RESPONSE SEEN WITH ISOPROTERENOL

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Purpose of Study: Intracellular Ca^{2+} overloading accompanies acute stressor states leading to an induction of oxidative stress, where prooxidants can overwhelm endogenous antioxidant defenses leading to tissue injury. Such an excessive intracellular Ca^{2+} accumulation is catecholamine-mediated and is intrinsically coupled to intracellular Zn^{2+} entry functioning as antioxidant. Herein, we hypothesized the acute stressor state associated with

isoproterenol administration, a synthetic catecholamine, would lead to hypozincemia with alterations in tissue Zn^{2+} , including heart, skeletal muscle, and liver.

Methods Used: Eight-week-old male Sprague-Dawley rats received subcutaneous administration of isoproterenol (Isop, 1 mg/kg). At 8 and 24 h and 7 days after Isop treatment, plasma Zn^{2+} was monitored, together with myocardial, skeletal muscle (rectus femoris) and hepatic tissue Zn^{2+} by atomic absorption spectroscopy. Untreated, age-/gender-matched rats served as controls.

Summary of Results: As compared to controls (101.6±3.3 µg/dL), hypozincemia ($p<0.05$) appeared at 8 h (55.0±2.9), but had resolved by 24 h (110.6±5.2) and remained normalized at 7 days (103.6±4.1). Compared to controls (85.1±2.1 µg/mg FFDT), cardiac Zn^{2+} levels were reduced ($p<0.05$) at 8 h (77.0±1.3) and 24 h (75.0±1.6), but were normalized by 7 days (83.5±1.3). In skeletal muscle, levels of Zn^{2+} (221.0±5.9 µg/mg FFDT) found in control tissue were reduced ($p<0.05$) at 8 h (195.0±4.1) and 24 h (197.5±9.0) and had returned toward normal levels at 7 days (203.0±4.1). On the other hand, hepatic Zn^{2+} content in control tissue was 85.2±2.6 µg/mg FFDT and increased ($p<0.05$) at 8 h (120.3±2.6) and 24 h (107.5±2.0) and remained elevated at 7 days (92.9±1.7).

Conclusions: Thus the acute stressor state induced by a catecholamine is accompanied by early hypozincemia, which quickly resolves and is associated with a decline in Zn^{2+} content of the heart and skeletal muscle. This contrasts to the liver, where tissue Zn^{2+} is increased as an early and persistent acute phase response over the course of 7 days and which may be based on an upregulated expression of metallothionein, a Zn -binding protein.

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A DYSHOMEOSTASIS OF MACRO- AND MICRONUTRIENTS IN PATIENTS HOSPITALIZED WITH ACUTE BURN INJURY

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Purpose of Study: The neurohormonal activation associated with congestive heart failure is accompanied by a dyshomeostasis of macro- and micronutrients resulting in a proinflammatory phenotype inextricably linked to a dysequilibrium in favor of prooxidants over endogenous antioxidant defenses. Such is also the case with acute burn injury, where divalent cation losses are likely to compromise antioxidant defenses, involving such metalloenzymes as Cu/Zn-superoxide dismutase (SOD), Mn-SOD, and Se-glutathione peroxidase. Herein, we investigated whether serum concentrations of these related divalent cations are adversely affected in patients hospitalized with acute burn injury.

Methods Used: In 187 patients (117M; 45±2 yrs) consecutively admitted to the Burn Unit of an urban medical center over the course of 3 yrs, we conducted a retrospective study of serum concentrations of Ca^{2+} , Mg^{2+} , Cu^{2+} , Zn^{2+} , Mn^{2+} , and Se^{2+} that had been obtained on hospital day 3–7.

Summary of Results: In this cohort of 187 patients, total burn surface area was 33±1% with 24±1% represented by third-degree burns. Hypocalcemia with serum Ca^{2+} <8.8 mg/dL was found in 95% while hypomagnesemia with serum Mg^{2+} <1.8 mg/dL was seen in 56%; reduced serum Cu^{2+} (<70 µg/dL) and Zn^{2+} (<75 µg/dL) were present in 45% and 76%, respectively; and reduced serum Mn^{2+} (<0.4 µg/dL) and Se^{2+} (<85 µg/dL) in 30% and 83%, respectively.

Conclusions: Our retrospective study reveals a simultaneous dyshomeostasis of multiple macro- and micronutrients in patients hospitalized with acute burn injury. Hypocalcemia together with severe hypozincemia and hyposelenemia are especially prevalent. The dyshomeostasis of Ca^{2+} and Zn^{2+} could be related to catecholamine- and parathyroid hormone (PTH)-mediated intracellular Ca^{2+} overloading, which is intrinsically coupled to intracellular Zn^{2+} entry and facilitated by upregulated expression of Zn^{2+} transporters and metallothionein, a Zn^{2+} -binding protein (Kamalov G, et al. *J Cardiovasc Pharmacol* 2009;53:414–423). This concerted disturbance in multiple essential divalent cations favors prooxidants over compromised antioxidant defenses leading to a proinflammatory phenotype.

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HYPOKALEMIA AND HYPOMAGNESEMIA WITH NEW ONSET ATRIAL FIBRILLATION IN HOSPITALIZED PATIENTS

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Purpose of Study: Among hospitalized patients, atrial fibrillation (AF) has reached epidemic proportions with increased risk of morbid and mortal cardiovascular events. Hence, the importance of preventable and correctable factors contributing to the appearance of AF, such as hypokalemia, hypomagnesemia or hypocalcemia, need to be addressed.

Methods Used: We retrospectively examined medical records covering a three consecutive month period (February to April, 2009) for patients hospitalized at an urban medical center, with or without cardiovascular disease, and whose discharge diagnoses included AF. We identified 39 patients with a history of known AF of which 13 (30%) were determined to have new onset sustained AF. We also examined their records for serum K^+ , Mg^{2+} and Ca^{2+} . Patients having other entities known to induce electrolyte abnormalities were excluded. These included: cirrhosis; diabetic ketoacidosis; the syndromes of Conn, Gitelman, Bartter and Cushing; renal tubular acidosis; an intestinal or biliary fistula; nasogastric suction; and parathyroid or thyroid disease.

Summary of Results: Of the 39 patients with AF (28 M; 54 ± 2 yrs), serum K^+ and Mg^{2+} were 3.9 ± 0.1 mEq/L and 2.0 ± 0.1 mg/dL, respectively, while serum Ca^{2+} was 8.9 ± 0.1 mg/dL. Using stringent criteria, however, hypokalemia (<4.0 mEq/L) was present in 56% and a comparable number had hypomagnesemia (<2.0 mg/dL) while 46% had both hypokalemia and hypomagnesemia. Hypocalcemia (<8.4 mg/dL) was not found in any of these patients (8.9 ± 0.1 mg/dL). In the 13 patients with new onset AF (8M; 58 ± 4 yrs), we found hypokalemia (3.6 ± 0.1) and hypomagnesemia (1.8 ± 0.01) with 91% having mild to moderate hypokalemia (≤ 3.6) and 53% hypomagnesemia (≤ 1.8).

Conclusions: Hypokalemia and hypomagnesemia, but not hypocalcemia, are common in hospitalized patients in whom new onset, sustained AF is found. Serum electrolytes should be carefully monitored, and when appropriate, promptly corrected with a view toward the prevention or correction of new onset AF.

81 PROLONGED QT_c INTERVAL WITH HYPOKALEMIA AND/OR HYPOMAGNESEMIA OF VARYING SEVERITY

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Purpose of Study: Hypokalemia and hypomagnesemia are critical electrolyte abnormalities associated with an enhanced risk of morbid and mortal events related to the appearance of cardiac arrhythmias. This is particularly the case when the heart's vulnerable period is increased by delayed myocardial repolarization, as suggested by QT_c interval prolongation on the electrocardiogram, and which can accompany these electrolyte abnormalities. Monitoring for QT_c prolongation therefore provides valuable ancillary information with which to gauge vulnerability to arrhythmias, but also to predict the likelihood of these electrolyte abnormalities. It has been previously suggested that electrocardiographic changes do not occur until serum K^+ levels are profoundly reduced (<2.6 mEq/L). This study was conducted to address whether prolonged QT_c (≥ 460 ms) would suggest the presence of hypokalemia and hypomagnesemia and where we defined hypokalemia as ≤ 3.6 mEq/L and hypomagnesemia as ≤ 1.8 mg/dL.

Methods Used: This retrospective study was conducted using the routine ECG obtained during July and August, 2009, in 149 patients (73 M; 54 ± 1 yrs) followed at an urban medical center with diverse illnesses and in whom QT_c was prolonged (≥ 460 ms) and where data on serum potassium and magnesium were available.

Summary of Results: Of the 149 patients with prolonged QT_c (524 ± 6 ms), 59 (40%) had hypokalemia (3.24 ± 0.04 mEq/L) and 33 (22%) had hypomagnesemia (1.65 ± 0.03 mg/dL) of mild to moderate severity while 15 patients (10%) had disturbances of both these electrolytes. More marked hypokalemia (<3.0 mEq/L) was found in 12 patients (2.67 ± 0.07 mEq/L) in whom QT_c was 498 ± 9 ms.

Conclusions: In addition to addressing increased risk of arrhythmias, a prolonged QT_c interval on routine electrocardiogram can prove useful in suggesting the presence of hypokalemia and/or hypomagnesemia, irrespective of their etiologic origins, and the need to monitor serum electrolytes. Prolongation of the QT_c is seen for hypokalemia and hypomagnesemia of varying severity, including when serum K^+ has fallen below 3 mEq/L.

82 INSULIN-LIKE GROWTH FACTOR-1 ATTENUATES OXIDATIVE STRESS INDUCED P53 EXPRESSION AND PREMATURE CELL SENESCENCE IN CULTURED HUMAN AORTIC ENDOTHELIAL CELLS

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Purpose of Study: There is increasing evidence that premature cell senescence is a potential cause of endothelium dysfunction, which in turn leads to vascular complications such as atherosclerosis. We have previously shown that IGF-1 attenuates atherosclerosis in apolipoprotein e deficient mice potentially via anti-inflammatory and anti-oxidant effects. In addition, we found that IGF-1 upregulates glutathione peroxidase 1 expression and reduces oxidized LDL induced reactive oxygen species formation in human aortic endothelial cells. In this study, we investigated the potential IGF-1 effect against premature senescence induced by oxidative stress in vascular endothelial cells.

Methods Used: Human aortic endothelial cells were incubated with human recombinant IGF-1 (0–100 ng/mL) for 24 hours, and then were exposed to hydrogen peroxide (100 μ M) for 1 hour. Cells were replated and the culture continued in endothelial growth medium for 7 days. Cell senescence was evaluated by quantifying senescence associated beta-galactosidase expressing cells. Western blot analysis was performed in parallel experiments after 7 days culture in endothelial growth medium.

Summary of Results: Hydrogen peroxide (100 μ M, 1 h) markedly increased beta-galactosidase positive cell number ($156 \pm 56\%$, $n=3$) and 100 ng/mL IGF-1 pretreatment completely abolished this increase ($-19 \pm 8\%$, $n=3$, $P < 0.05$). The tumor suppressor gene, p53, is known to be involved and upregulated in conditions of cellular senescence. One hour exposure to hydrogen peroxide caused a marked 8-fold increase in p53 protein expression after 7 days, and IGF-1 pre-incubation blocked this increase in p53 by 65%. A monoclonal antibody against IGF-1 receptor (alpha-IR3), which can compete for IGF-1 binding to the IGF-1 receptor, markedly inhibited the ability of IGF-1 to rescue cells from hydrogen peroxide upregulation of p53 and increase in cell senescence.

Conclusions: IGF-1 markedly inhibits oxidative stress induced p53 upregulation and cellular senescence and this effect could play an important role in the ability of IGF-1 to prevent endothelial dysfunction and atherosclerosis progression.

83 DIFFERENTIAL REGULATION OF UBIQUITIN LIGASES ATROGIN-1 AND MURF-1 IN ANGIOTENSIN II-MEDIATED SKELETAL MUSCLE ATROPHY

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Purpose of Study: Advanced congestive heart failure is associated with activation of the renin-angiotensin system and skeletal muscle atrophy. Angiotensin II (Ang II) infusion in mice produces cachexia secondarily to increased muscle proteolysis and also decreased levels of circulating and skeletal muscle IGF-1. Two E3 ubiquitin ligase genes Atrogin-1 and MuRF-1 are known to be upregulated in skeletal muscles of Ang II-infused animals and are important in mediating skeletal muscle proteolysis via the ubiquitin-proteasome system (UPS). The purpose of this study is to determine mechanisms linking Atrogin-1 and MuRF-1 expression and IGF-1 signaling.

Methods Used: Expression of Atrogin-1, MuRF-1 was analyzed in skeletal muscles of Ang II infused mice by quantitative RT-PCR. Plasmid vectors which contain promoter regions of Atrogin-1 and MuRF-1 upstream of the luciferase reporter gene were electroporated into mouse gastrocnemius muscle and luciferase activity was measured after Ang II infusion.

Summary of Results: Expression of Atrogin-1 and MuRF-1 were elevated one day after the initiation of Ang II-infusion (4.92 ± 0.86 and 7.82 ± 2.02 fold, respectively). Contrary to wild-type (WT) mice, there was no significant reduction of skeletal muscle weight in mice overexpressing IGF-1 specifically in skeletal muscle (MLC/Igf-1 mice) infused with Ang II. In skeletal muscles of MLC/Igf-1 mice, the basal and Ang II-induced expression of Atrogin-1, but not MuRF-1, was significantly repressed compared to WT mice. In vivo electroporation-mediated reporter gene assay showed that the activation of these ubiquitin ligase genes by Ang II is mediated by 1 kbp and 5 kbp

upstream promoter regions of Atrogin-1 and MuRF-1, respectively. IGF-1 overexpression in skeletal muscle suppressed Atrogin-1 (1kbp) promoter activity, but not MuRF-1 (5kbp) activity. Furthermore, the 500 bp upstream region of Atrogin-1 promoter was responsible for this IGF-1 mediated reporter gene suppression.

Conclusions: These data demonstrate that prevention of Ang II induced atrophy by IGF-1 is mediated via the ability of IGF-1 to repress Atrogin-1 expression, rather than MuRF-1. The 1kbp and 500 bp upstream promoter regions of Atrogin-1 are responsible for Ang II-mediated activation and IGF-1 mediated suppression of Atrogin-1, respectively.

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ADULT LEFT VENTRICULAR MASS IS ASSOCIATED WITH LONG-TERM BLOOD PRESSURE VARIABILITY BEGINNING IN CHILDHOOD IN BLACKS, BUT NOT IN WHITES: THE BOGALUSA HEART STUDY

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Purpose of Study: Blood pressure (BP) is a very labile physiologic parameter in health and disease. Increased 24-hour ambulatory BP variability is associated with severity of end-organ damage and a higher rate of cardiovascular events, even after adjusting for levels. This study assessed the hypothesis that long-term BP variability from childhood to adulthood, besides levels, is predictive of adulthood left ventricular mass (LVM).

Methods Used: The longitudinal study cohort consisted of 1053 subjects (718 whites and 335 blacks; 42% males; age = 24–48 years; mean age = 38.4 years) enrolled in the Bogalusa Heart Study. Study subjects were examined serially 4–14 times for BP from childhood to adulthood over an average of 19.7 years follow-up, since 1973, with 8515 observations of BP. Echocardiography was performed in adulthood between 2001 and 2009. The BP variability from childhood to adulthood was measured as long-term variability from mean levels.

Summary of Results: Blacks versus whites showed significantly greater BP variability (mmHg) (9.1 vs 6.7 for systolic BP, $p<0.001$ and 8.0 vs 6.6 for diastolic BP, $p<0.001$) and higher LVM index (gram/height in $m^2.7$) (38.8 vs 35.4, $p<0.001$). In multivariable regression analyses, adjusting for age, sex, body mass index, LDL cholesterol, glucose, and the average long-term BP levels, LVM index ($g/m^2.7$) in adulthood was significantly associated with systolic BP variability (mmHg) (regression coefficient $\beta=0.66$, $p<0.001$) and diastolic BP variability (mmHg) ($\beta=0.81$, $p<0.001$) in blacks, but not in whites. Importantly, the standardized regression coefficients of the BP variability were greater than those of long-term BP levels ($\beta=0.23$ vs $\beta=0.11$ for systolic BP; $\beta=0.22$ vs $\beta=0.06$ for diastolic BP).

Conclusions: These findings indicate that long-term BP variations reflecting stimulus-response characteristics are predictive of left ventricular hypertrophy in adulthood, independent of BP levels, among black individuals, which may have implications for preventive cardiology.

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SERUM PHOSPHORUS LEVELS ARE ASSOCIATED WITH CAROTID INTIMA-MEDIA THICKNESS IN ASYMPTOMATIC YOUNG ADULTS: THE BOGALUSA HEART STUDY

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Purpose of Study: Elevated serum phosphorus has been associated with increased mortality from cardiovascular (CV) disease. However, information is scant regarding the influence of serum phosphorus within the normal range on vascular risk in terms of subclinical atherosclerosis in asymptomatic young adults.

Methods Used: Serum phosphorus along with other CV risk factor variables were measured in 856 white and 354 black subjects without known CV disease or renal disease. Carotid intima-media thickness (IMT) was measured by B-mode ultrasonography.

Summary of Results: Significant race and sex differences were noted for serum phosphorus (blacks>whites) and carotid IMT (black females>white females; males>females). In bivariate analyses, serum phosphorus was correlated with carotid IMT ($p<0.001$); and smokers showed higher

phosphorus levels than nonsmokers ($p=0.008$). In multivariable regression analyses, carotid IMT was significantly associated with serum phosphorus (regression coefficient $\beta=0.028$, $p<0.001$) and smoking ($\beta=0.032$, $p<0.001$), adjusting for other CV risk factors and estimated glomerular filtration rate. In addition, a significant interaction effect of cigarette smoking and serum phosphorus on carotid IMT was noted, with a greater increasing trend of carotid IMT with phosphorus in smokers than that in nonsmokers ($p=0.019$ for interaction).

Conclusions: Serum phosphorus within the normal range is an important correlate of carotid IMT in asymptomatic young adults, with smoking potentiating this adverse association.

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THE ASSOCIATION OF BIRTH WEIGHT WITH BLOOD PRESSURE IS AMPLIFIED WITH INCREASING AGE: THE BOGALUSA HEART STUDY

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Purpose of Study: The adverse relationship between low birth weight and blood pressure levels in adulthood is generally accepted; however, a recent debate has focused on whether increasing age amplifies this trend. The current study tested this aspect as part of the Bogalusa Heart Study.

Methods Used: The study cohort included 6875 individuals (61.7% whites and 38.3% blacks; 40.3% males) who were examined 1–12 times for blood pressure from childhood to adulthood, with 25521 observations. Information on birth weight and gestational age was obtained from Louisiana birth certificates.

Summary of Results: Blacks versus whites and females versus males showed significantly lower birth weight. In the combined sample of blacks and whites, after adjusting for race, sex, age and gestational age, low birth weight (kg) was associated with higher systolic blood pressure levels (mmHg) in adolescence (aged 12–17 years, regression coefficient $\beta=-0.88$, $p<0.001$) and adulthood (aged 18–48 years, $\beta=-1.66$, $p=0.003$), but not in preadolescence (aged 4–11 years, $\beta=-0.10$, $p=0.624$). Adjustment for current body mass index yielded considerably stronger association. Moreover, the strength of the birth weight-systolic blood pressure relationship, measured as regression coefficients, was amplified with increasing age ($p<0.0001$ for trend), regardless of adjustment for current body mass index. Further, the strengthened association which resulted from adjustment for current body mass index was closely related to the birth weight-body mass index and body mass index-systolic blood pressure correlations, especially in childhood.

Conclusions: Since age is an overall indicator of long-term environmental burden, these findings on the potentiating effect of increasing age on the birth weight-blood pressure relationship suggest that the fetal programming related to intrauterine malnutrition and the increasing cumulative burden with age of unhealthy life-style behaviors affect the development of adult hypertension in a synergistic manner.

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RELATIONSHIP BETWEEN SOCIOECONOMIC VARIABLES AND DEPRESSION WITH C - REACTIVE PROTEIN IN BOGALUSA HEART STUDY

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Purpose of Study: CRP is a nonspecific inflammatory marker but has been useful in prognosticating various disease states especially cardiovascular disease. Treatments that lower cardiovascular risk have been found to also lower circulating CRP. In this study we chose to look at the psychosocial and lifestyle variables as they predict circulating CRP.

Methods Used: The Bogalusa heart study is a unique biracial population of men and women who have been followed prospectively for nearly 40 years. We analyzed several variables including depression, yearly salary, physical activity and domiciliary ownership. We noted a statically significant relation between these variables and CRP. We incorporated them into a linear prediction model that included sex, body size and lipids. These variables remained as contributing to variance to the circulating CRP between subjects.

Summary of Results: A total of 1195 subjects were examined in 4 subgroups (<\$5000, 15,001–30,000, 30,001–45,000 and >45,000). There was a statistically significant higher mean CRP in subjects with reported income< 30,000

($p < 0.001$). Self reported income was also inversely correlated with depression ($r = -0.389$; $p < 0.0001$). A total of 1211 subjects were evaluated based on domiciliary ownership. Subjects reporting renting as compared to owning a home had mean higher CRP and higher depression scores ($p < 0.0001$). Self reported physical activity and television hours per week were also noted to have inverse relationship with CRP when assessed by ANOVA.

Conclusions: Our study confirms depression and psychosocial status as potentially being important mediators of underlying inflammation commonly associated with atherosclerosis.

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RELATIONSHIP BETWEEN PSYCHOSOCIAL VARIABLES AND ADIPONECTIN IN BOGALUSA HEART STUDY

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Purpose of Study: Adiponectin is a protein marker implicated in the pathophysiology of cardiovascular disease. In general, conditions associated with an increased adiponectin are related to a decreased cardiovascular risk. In this study we chose to look at the psychosocial variables as measured on standardized questionnaires that assessed relatedness to others, hostility as they predict circulating adiponectin.

Methods Used: The Bogalusa heart study is a unique biracial population of men and women who have been followed prospectively for nearly 40 years. We analyzed psychosocial variables including hostility and sense of belonging. We noted a statically significant relation between these variables and adiponectin. We incorporated these variables into a prediction model that included age, sex, insulin resistance, body size and lipids, these variables remained as contributing variance to the circulating adiponectin.

Summary of Results: We studied a total of 1203 subjects. We found that Women have higher adiponectin levels compared to men. Caucasians have higher adiponectin levels than African Americans. Hostility, Insulin Resistance, Waist circumference and lipids (TC/HDL) are found to be inversely related to adiponectin whereas sense of belonging is positively correlating with adiponectin ($p < 0.0001$).

Conclusions: Our study suggests that self reported social interaction as measured by questionnaires is related to an increased level of adiponectin. This finding supports the importance of psychosocial factors being associated with novel markers that are helpful in predicting cardiovascular risk.

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SECONDARY HYPERPARATHYROIDISM IN AFRICAN-AMERICANS WITH DECOMPENSATED BIVENTRICULAR FAILURE

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Purpose of Study: Disturbances in Ca^{2+} balance accompany the aldosteronism associated with congestive heart failure (CHF). In African-Americans with CHF, Ca^{2+} balance can be further compromised by the prevalence of vitamin D deficiency, where the greater melanin content of skin acts as a natural sunscreen, and lactose intolerance with reduced dairy/dietary Ca^{2+} . High dietary Na^+ , which is calciuric, hypoalbuminemia, and a loop diuretic are also contributory. We previously reported (Alsafwah S, et al. *Am J Med Sci* 2008;335:292-7) on elevated serum parathyroid hormone (PTH) in keeping with secondary hyperparathyroidism (SHPT) in 58 African-American (AA) men and women (51 ± 1 yrs) hospitalized with decompensated biventricular failure due to a dilated cardiomyopathy with reduced ejection fraction (EF; $< 35\%$) and in whom reduced serum 25(OH)D levels (< 30 ng/mL) were also present. This contrasted to AA with comparable EF and hypovitaminosis D, but without CHF, to implicate these additional factors in compromising Ca^{2+} balance and predisposing to SHPT. We now routinely monitor serum PTH and 25(OH)D as a standard of care in these AA patients with CHF and treat their vitamin D deficiency using either casual sunlight exposure and/or a regimen that includes weekly 50,000 IU ergocalciferol (Zia A, et al. *J Invest Med* 2009;57:322-3). Herein we report on SHPT in a larger cohort of AA hospitalized here in Memphis (latitude 35°N) with decompensated failure.

Methods Used: In this retrospective study, we collected the results of serum PTH and 25(OH)D, together with serum albumin, that had been routinely monitored in 188 AA (134 M; 51 ± 1 yrs) hospitalized with decompensated biventricular failure due to a dilated cardiomyopathy with reduced EF.

Summary of Results: We found elevated serum PTH (119 ± 7 pg/mL), which exceeds the upper limit to the normal reference range (65 pg/mL), together with hypovitaminosis D (14 ± 11 ng/mL) and hypoalbuminemia (2.90 ± 0.06 g/dL).

Conclusions: SHPT and vitamin D deficiency are common findings in AA hospitalized with decompensated biventricular failure and where hypoalbuminemia may reflect a protein-losing enteropathy associated with splanchnic congestion (Battin DL, et al. *Am J Med Sci* 2010 (In press)).

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THE RELATION OF PERIPHERAL ARTERIAL TONOMETRY MEASUREMENTS TO BLOOD PRESSURE IN AFRICAN AMERICANS: THE JACKSON HEART STUDY

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Purpose of Study: Measurements of digital vascular tone and function by peripheral arterial tonometry (PAT) is novel and is associated with traditional cardiovascular risk factors in non-Hispanics whites. There is limited data on PAT in African Americans (AA) despite the disproportionate prevalence of hypertension and hypertension-related cardiovascular morbidity and mortality in this group. In this study, we examined the association of digital vascular tone and function to systolic and diastolic blood pressure (SBP and DBP, respectively) in AA.

Methods Used: Measurements of PAT were collected between October 2007 and July, 2009 on a subset of Jackson Heart Study participants ($n = 699$; mean age, 57 ± 12 years; 60% women) using a finger tip tonometry device (EndoPAT2000). The sensor was placed on the forefinger, and PAT measures were obtained at baseline and during reactive hyperemia induced by 5-minute forearm BP cuff occlusion. The vascular response post-occlusion relative to baseline was evaluated and expressed as the PAT ratio (natural logarithm of the ratio of post-deflation to baseline pulse amplitude in the hyperemic finger divided by the same ratio in the contralateral finger that served as control).

Summary of Results: After adjustment for the traditional cardiovascular risk factors, we found a significant and inverse relation of the PAT ratio to both SBP ($p = 0.0008$) and DBP ($p < 0.0001$). For every 1 SD change in SBP and DBP there was a decrement in PAT ratio of 7% and 9%, respectively. Baseline pulse amplitude was significantly and positively related to DBP ($p = 0.0008$). Every 1 SD increase in DBP was accompanied by a 19% increase in baseline pulse amplitude. In a stepwise multivariable linear regression analysis, SBP and DBP jointly accounted for 3.5% and 2.1% of variation in PAT ratio and baseline pulse amplitude, respectively.

Conclusions: We have confirmed a significant relation between digital vascular tone and function measured by PAT and both SBP and DBP in AA. Further studies are warranted to investigate the utility of these measurements in predicting the onset of hypertension and cardiovascular outcomes in this high risk population.

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PLASMA BRAIN NATRIURETIC PEPTIDE LEVELS IN HOSPITALIZED PATIENTS WITH AND WITHOUT PRESERVED EJECTION FRACTION

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Purpose of Study: Plasma brain natriuretic peptide (BNP) levels are generally monitored to address abnormal elevations of this peptide that accompany central congestion due to the intravascular and intracardiac volume expansion attendant with hormonally mediated salt and water retention. This homeostatic response is invoked in response to reduced renal perfusion associated with either systolic or diastolic heart failure. These elevations in BNP also reflect atrial and ventricular chamber distention, with or without hypertrophy, and which may accompany diastolic dysfunction with preserved ejection fraction (EF) or systolic dysfunction with reduced EF. Herein we addressed plasma BNP levels in patients with and without reduced EF.

Methods Used: This retrospective study examined plasma BNP levels obtained in patients admitted to an urban medical center inpatient service during May, 2009, and in whom echocardiographic surveillance had identified either reduced EF ($\leq 35\%$) or preserved EF ($> 50\%$), together with diastolic dysfunction by Doppler E/A ratio, left ventricular hypertrophy (LVH), and/or left atrial enlargement (LAE).

Summary of Results: Sixteen patients (14M; 54.6±1.9 yrs) were found to have reduced EF (23.4±1.8%), due to a dilated cardiomyopathy, together with elevated plasma BNP (1018±235 pg/mL; range 96-3320) and which was markedly elevated (>400 pg/mL) in 11 pts (1307±271 pg/mL). Fourteen patients (12M; 55.3±3.1 yrs) having preserved EF (60.8±2.2%), together with LVH, LAE and/or diastolic dysfunction, were identified and in whom plasma BNP was also elevated (244±63 pg/mL; range 10-683 pg/mL) exceeding the normal reference range (>100 pg/mL) in 9 patients (355±75 pg/mL) while exceeding 400 pg/mL in only 3 patients.

Conclusions: Abnormal elevations in plasma BNP are found in patients with and without preserved EF. However, the extent to which plasma BNP is elevated in patients with reduced EF is greater ($p<0.05$) than those levels seen with preserved EF, where diastolic dysfunction, LVH and/or LAE may each be contributory.

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CORRELATION OF EF MEASURED BY MUGA SCAN AND ANGIOGRAM IN PATIENTS WITH ATRIAL FIBRILLATION, DEPARTMENT OF MEDICINE

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Purpose of Study: Precise assessment of left ventricular ejection fraction (LVEF) has implicit immense connotation in the epoch of automatic implantable cardioverter defibrillators (AICDs), and a low EF may be one of the solitary deciding factor in determining AICD implantation in certain patient populations. We sought to see the accuracy of LVEF measured by different methods in patients with and without atrial fibrillation.

Methods Used: There are various methods, invasive and noninvasive, which can help to calculate EF. We sought to conduct a retrospective study comparing EF in patient with and without atrial fibrillation by invasive (angiography) and noninvasive methods (MUGA) in 200 patients in our hospital from 2005–2007. We used Grouped T test to test for a statistically significant difference between the two methods of EF measurement in each group of patients.

Summary of Results: In Patients with atrial fibrillation we found a positive correlation between MUGA and Coronary angiogram and R2 value is 0.8989 with the intercept as -4.47 and the 95% confidence interval for this is -7.46 to -1.48 and P value was found to be 0.0037. The X variable has coefficient of 0.95. The 95% confidence interval is 0.88 through 1.01 and P value 0.000. For patients without atrial fibrillation the R2 value was 0.98 with intercept -1.95 and 95% confidence interval of -3.06 to -0.83 . In this group P value was 0.0008 and X variable had the coefficient of 1.02, with 95% confidence interval of 0.99 through 1.04 and the P value being 0.0000.

Conclusions: In cases of patients without atrial fibrillation there is no statistically significant difference between MUGA and Angiogram with P value of 0.54296. Although in patients with atrial fibrillation there was significant difference between the two techniques to estimate EF with P value of 0.0038. Atrial fibrillation has significant effect on EF estimation by two different methods.

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CORONARY INTERVENTIONS BASED ON FRACTIONAL FLOW RESERVE: A META-ANALYSIS

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Purpose of Study: Fractional Flow Reserve (FFR) measurement has been used in the assessment of intermediate coronary lesions (40%–70%). The routine use of FFR has not been accepted. The purpose of this study was to determine the outcomes observed in multiple laboratories to attempt to find an overall estimate of the effects of FFR guided coronary interventions.

Methods Used: Systematic review of available published articles on FFR based interventions with at least one year follow up, with defined major adverse cardiac effects (MACE) as endpoints were included in this meta-analysis. All patients in these studies were divided into either FFR managed group or, intervention group. Out of 195 studies only 14 studies were selected

based on the type of study, patient selection, and availability of all cause mortality data.

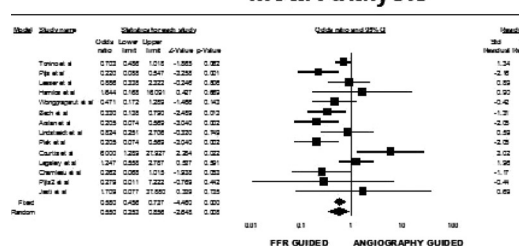
Summary of Results: (1) There were 1547 patients in the deferral group and 1220 patients in the intervention group. Mean age in the deferral group was 64±2.2 years and in the intervention group 65±4.8 years. Combined events in first year follow up in the FFR managed deferred group were 164 and in the Intervention group was 217. (2) Metaanalysis calculated Forrest plot is as follows:

METAANALYSIS

FFR GUIDED ANGIOGRAPHY GUIDED

Conclusions: (1) The analysis shows that despite variable study methods FFR guided therapy appears to result in more favorable patient outcomes. (2) We conclude that FFR guided angioplasty may reduce MACE. (3) Additional randomize studies of FFR with co-morbidities such as renal disease and diabetes are needed.

Meta Analysis



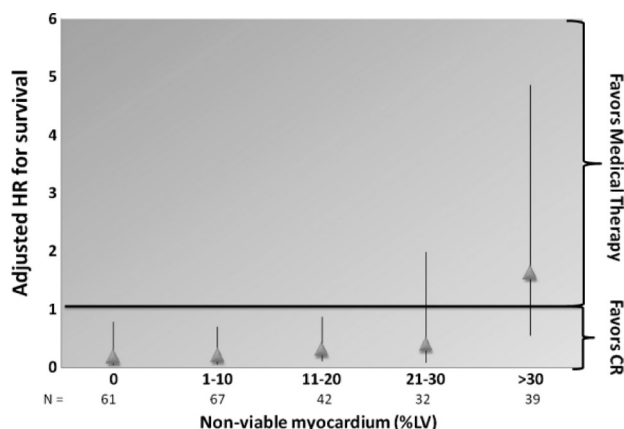
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VIABILITY ASSESSMENT USING AUTOMATED QUANTITATIVE ANALYSIS OF THALLIUM-201 MYOCARDIAL PERFUSION IMAGING

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Purpose of Study: To determine the value of using an automated quantitative analysis of myocardial perfusion imaging in patients with ischemic cardiomyopathy (ICM).

Methods Used: We identified ICM patients who had rest-redistribution thallium-201 myocardial perfusion imaging (MPI). Perfusion defects were assessed by automated method. Regions with <50% activity vs. normal were considered non-viable. Mortality was verified against the social security death index database.



Summary of Results: Of 246 patients, 37% underwent coronary revascularization (CR) within 3 months of MPI. Independent predictors of CR

included chest pain and transient ischemic left ventricular (LV) dilatation while a prior history of CR or ventricular arrhythmias favored medical therapy (MT). During 41 ± 30 months of follow-up 45% died. Survival was better with CR than MT ($P < 0.0001$). For CR but not MT, survival was better for those with a smaller area of non-viable myocardium (risk of death increased by 5%/1% increase in non-viable myocardium, $P = 0.009$). CR had a mortality advantage over MT when non-viable myocardium was $\leq 20\%$ LV but not larger with a trend towards harm with CR when non-viable myocardium $> 30\%$ LV (Fig).

Conclusions: Automated quantitative analysis of MPI is useful in predicting survival in ICM, but the decision for or against CR is a complex one as it depends on multiple other factors and "viability testing" is just one variable that needs to be incorporated in the decision making process.

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DEMOGRAPHIC AND CLINICAL CHARACTERISTICS PREDICTING ECG PARAMETERS AMONG NORMAL ADULT POPULATION

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Purpose of Study: Studies suggest basic electrocardiogram (ECG) interval and amplitude may differ by different demographic and co-morbid condition among healthy adults without pre-existing coronary artery disease or conduction problem. However, magnitude of the combined effect of these characteristics are not well defined.

Methods Used: Data from NHANES III ($n = 8561$, 1988–1994) were used to determine the demographic and clinical predictors of different ECG parameters. 5617 participants were included in the final analysis after excluding people with probable or possible myocardial injury and other than sinus rhythm. Different ECG parameters were calculated across demographic characteristics and statistical significance of differences were determined using least squared means and maximum likelihood ratio for continuous and categorical variables, respectively. Association of prolonged PR interval between these characteristics were determined by using a multivariate adjusted logistic regression model.

Summary of Results: PR interval is significantly higher among age ≥ 75 years, male gender, black race, non-smokers, obese and hypertensives (all p -value are < 0.05). Older people (age ≥ 75 years) has higher prevalence of prolonged PR interval (PR interval > 200 msec) than younger adults (16.9% vs. 6.50%, respectively). Prevalence of prolonged PR interval were also significantly higher among male, black, non-smokers and hypertensives. Odds ratio (95% CI) of prolonged PR interval was 2.82 (1.98–4.01) among older compared to younger population. The analogous odds ratios (95% CI) were 1.51 (1.13–2.03) among male (vs. female), 1.71 (1.27–2.30) among black (vs. white) and 1.64 (1.22–2.22) among obese (vs. non-obese) (each p -value < 0.01). Interestingly there was no association between prolonged PR interval by hypertension and diabetes (OR: 1.09 (0.83–1.44) and 1.16 (0.76–1.77), respectively).

Conclusions: Among US adults, ECG parameters vary by demographic characteristics. Demographic profile rather than pre-existing comorbid conditions are more likely to influence ECG intervals among healthy adult individual. Further studies are warranted to define and modify ECG interpretation based on these characteristics.

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CRITICAL LIMB ISCHEMIA: DOES PATENCY MATTER?

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Purpose of Study: Background: In critical limb ischemia (CLI), an underlying principle of treatment is that it takes more oxygenated blood to heal a wound than to maintain tissue integrity. Hence, long-term patency of the target vessel is usually not a treatment goal. However, limited surgical data suggest that long-term graft patency is associated with improved outcomes. Whether this principle translates to percutaneous therapy for CLI is not known.

Methods Used: Methods: Patients (P) who underwent infrapopliteal revascularization from 2007–2009 were identified from the Ochsner catheterization laboratory. Those with CLI formed the study population.

The rate of prior ipsilateral target limb revascularization for CLI was determined.

Summary of Results: Results: Among 29 P, 10 (35%) presented with rest pain and 19 (65%) had ulcers (Table 1). 14 P underwent percutaneous balloon angioplasty (48%) and 15 P (52%) had stents deployed (60% bare metal and 40% drug eluting). Procedural success was 96.5%. Six P (20%) had a history of prior ipsilateral revascularization for CLI (Table 2).

Conclusions: Conclusion: One in 5 P undergoing infrapopliteal angioplasty for CLI have had a similar procedure in the past. Percutaneous techniques to maintain long-term patency might, reduce the recurrence of CLI.

TABLE 1

VARIABLE (%)	STUDY POPULATION N=29
Age $\pm$ SD	72 $\pm$ 15.1
Race (Caucasian)	20 (69)
Body Mass Index $\pm$ SD	28 $\pm$ 5.4
Hypertension	28 (97)
Diabetes	16 (55)
History of coronary artery disease	19 (66)
Hyperlipidemia	25 (86)
Current Smoker	4 (14)
History of Amputation	4 (14)
History of Chronic Kidney Disease	12 (41)
LVEF $\leq$ 40%	7 (24)

LVEF=left ventricular ejection fraction

TABLE 2

PATIENT	TIME PERIOD BETWEEN INTERVENTIONS	SUPERFICIAL FEMORAL ARTERY	POPLITEAL ARTERY	ANTERIOR TIBIAL ARTERY	TIBIOPERONEAL ARTERY	POSTERIOR TIBIAL ARTERY
No 1	6 months					BMS
No 2	4 years	BMS	BMS		DES	
No 3	3 years	BMS				
No 4	5 months	BMS	BMS			
No 5	3 years		DES		DES	
No 6	4 months		PTA	PTA		

PTA=percutaneous angioplasty, BMS=bare metal stent, DES=drug eluting stent

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HEMODYNAMIC EFFECTS OF ANGIOTENSIN RECEPTOR BLOCKADE IN HYPERTENSIVE RATS

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Purpose of Study: Hemodynamic effects of angiotensin II receptor antagonist (ARB) telmisartan (T) was determined in spontaneously hypertensive rats (SHR).

Methods Used: 16 male SHR divided into two groups (8 rats/group). Group 1 was control; group 2 was given T (10 mg/kg/day) in drinking water for 12 weeks. At the end, rats were anesthetized with pentobarbital and carotid artery was cannulated with a transducer tipped catheter advanced to left ventricle (LV) to determine global contractility (dP/dtmax and dP/dtmin). Millar catheter replaced with polyethylene tubing (PE-50) advanced into LV, jugular vein, and femoral artery for determination of systemic, coronary and renal hemodynamics using radiolabeled microspheres. Heart, lungs, and kidneys were removed, weighed and counted.

Summary of Results: T decreased LV weight compared to placebo (Table 1). Systemic hemodynamics improved as mean arterial pressure and total peripheral resistance decreased. Coronary and renal hemodynamics improved as vascular resistances decreased and flow reserve increased. Renal hemodynamics improved as renal vascular resistance decreased. Diastolic dysfunction was corrected as maximal rate of pressure rise and diastolic time constant decreased.

Conclusions: T produced significantly improved systemic hemodynamics, heart function and LV weight in SHR. These data demonstrate that ARB with T was effective hemodynamically producing beneficial cardiovascular and renal effects.

TABLE 1

	Control SHR (placebo)	Treated SHR (telmisartan 10 mg/kg/day)
Left Ventricular Weight Index (mg/g)	3.35 ± 0.03	2.06 ± 0.04*
Mean Arterial Pressure (mm Hg)	188 ± 6	101 ± 5*
Total Peripheral Resistance (units)	0.764 ± 0.032	0.427 ± 0.054*
Cardiac Index (ml/min/kg)	249 ± 13	231 ± 12
Coronary Flow Reserve (ml/g/min)	5.80 ± 0.71	9.12 ± 0.63*
Coronary Vascular Resistance (units)	33.28 ± 3.23	16.33 ± 1.58*
Minimal Coronary Vascular Resistance (units)	15.26 ± 1.43	9.34 ± 0.76*
Renal Blood Flow (ml/min)	6.89 ± 0.40	7.21 ± 0.38
Renal Vascular Resistance (units)	27.85 ± 1.55	13.22 ± 1.12*
Maximal Rate of Pressure Rise (mmHg/sec)	9876 ± 1055	1132 ± 976
Maximal Rate of Pressure Decline (mmHg/sec)	-7967 ± 833	-9231 ± 765*
Diastolic Time Constant (Tau) (ms)	13.2 ± 1.1	9.1 ± 0.5*

Values mean ± 1 SEM; *p<0.05

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STROKE VOLUME DURING EXERCISE IS ASSOCIATED WITH INSULIN SENSITIVITY AMONG WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Purpose of Study: Polycystic Ovarian Syndrome (PCOS) is a common disorder of elevated total testosterone (TT), irregular menses and insulin resistance. During exercise, lower peak oxygen uptake (VO₂max) has been observed in PCOS compared to healthy controls. It is not clear if lower VO₂max is due to elevated TT or lower insulin sensitivity (IS), which correlates with lower VO₂max in healthy women. We sought to determine: 1) if VO₂max, cardiac output (CO), and stroke volume (SV) during exercise were different between women with PCOS and controls with the metabolic syndrome (MetS); and 2) if VO₂max, CO, SV correlated with IS and/or TT. **Methods Used:** Nine pre-menopausal, obese women with MetS with and without PCOS were recruited. IS was determined during an intravenous glucose tolerance test. VO₂max, SV, CO were obtained during a modified Astrand-Saltin treadmill protocol using foreign gas rebreathing technique (C2H₂). Data were collected at rest, during two steady state periods at a comfortable speed and at peak stress. SV and CO were indexed by body surface area.

Summary of Results: There was no significant difference in age (PCOS:35±7, MetS:37±6, p = 0.6) or body mass index (PCOS:37.1±6, MetS:34.7±4kg/m², p = 0.5) between PCOS or controls. During exercise, there was no significant difference in VO₂max (PCOS:22±4, MetS:21±1.4ml/kg/min, p = 0.8) or CO and SV. Analyzing all women together, there were significant positive correlations of IS and SV during

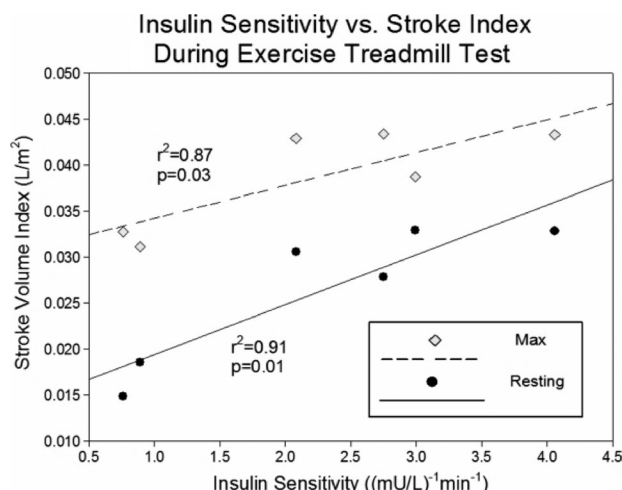


FIGURE 1

exercise (Figure 1). There was no association of VO₂max, CO or SV with TT. **Conclusions:** SV during exercise correlates with IS among women with PCOS and/or the MetS. Poor-fitness in PCOS is not associated with TT but strongly influences IS.

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CLINICAL AND LABORATORY PHENOTYPES OF STATIN-INTOLERANT PATIENTS

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Purpose of Study: Muscle pain, without elevated plasma creatine phosphokinase (myalgia), occurs in up to 10% of patients prescribed statins. This has emerged as a significant barrier to effective treatment of hyperlipidemia. The etiology and predisposing factors for statin-induced myalgia are not clearly understood.

Methods Used: We conducted a case-control study to define the clinical and laboratory phenotype of patients referred to the VA Lipid Clinic for evaluation of statin intolerance. The phenotype of statin-intolerant (SI) patients (n = 55) was compared to that of statin-tolerant (ST) patients identified from the referral population (n = 165).

Summary of Results: SI patients were more likely to be Caucasian and exhibited a higher prevalence of musculoskeletal disease and prior history of muscle pain. Neither plasma creatine phosphokinase (CPK), electrolytes nor indices of hepatic, renal or thyroid function were altered in SI patients. SI patients were more likely to have concomitant treatment with other lipid medications, including gemfibrozil, nicotinic acid and ezetimibe. SI patients were also more likely to be treated with aspirin and digoxin. Myalgia resolved following discontinuation of the index statin in 94.6% of SI patients and recurred with rechallenge in 58.2%. Seventy-two % of SI patients had a history of intolerance to 2 or more statins. Only slightly more than half (55.6%) of SI patients tolerated alternative statin therapy and were more likely to be treated with non-statin lipid medication. Consequently, as compared to ST patients, SI patients exhibited higher levels of LDL-C (134.5 vs. 99.7 mg/dL) and triglyceride (181.9 vs. 137.2 mg/dL).

Conclusions: Statin-intolerant patients exhibit a distinctive clinical phenotype. Conventional predictors of statin-induced myositis are not altered in SI patients with myalgia. As a consequence of their inability to tolerate statin therapy, the control of atherogenic lipids is compromised in SI patients.

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RETINOIC ACID RECEPTOR-α SIGNALING ENHANCES THE TRANSCRIPTION AND EXPRESSION OF NATRIURETIC PEPTIDE RECEPTOR-A GENE IN MOUSE MESANGIAL CELLS

P. Kumar, G. Bolden, KN. Pandey Tulane University Health Sciences Center and School of Medicine, New Orleans, LA.

Purpose of Study: Activation of guanylyl cyclase/natriuretic peptide receptor-A (GC-A/NPRA) by cardiac hormones atrial and brain natriuretic peptides produces the second messenger cGMP, which activates downstream signaling and biological effects of NPRA including vasorelaxation, anti-mitogenic, and anti-hypertrophic effects. The objective of the present study was to gain insight into the signaling mechanism of all-trans retinoic acid (ATRA) in the regulation of Npr1 (coding for GC-A/NPRA) gene transcription and expression in cultured mouse mesangial cells.

Methods Used: Cells were cultured in Dulbecco's modified Eagles medium (DMEM) containing 10% fetal bovine serum and ITS (insulin, transferrin, and sodium selenite) and were transiently transfected using Lipofectamine-2000. Role of retinoic acid receptor α (RARα) in ATRA-mediated signaling in Npr1 gene transcription and expression was studied by luciferase assay, real time RT-PCR, and sequential chromatin immunoprecipitation assay (ChIP).

Summary of Results: The results showed that ATRA significantly increased Npr1 mRNA, NPRA protein expression, and intracellular accumulation of cGMP in a dose-dependent manner. Furthermore, deletion of the Npr1 promoter from the region -365 to +55 base pairs caused a 7-fold increase in luciferase activity. ATRA-dependent Npr1 gene transcription was effectively inhibited by Ro 41-5253, a specific antagonist for RARα. Over expression of RARα significantly increased ATRA-dependent luciferase activity of Npr1 gene promoter. ATRA also enhanced *in vivo* binding of Ets-1 to Npr1 promoter as confirmed by ChIP assays. Moreover, sequential ChIP

assay showed simultaneous presence of RAR α and Ets-1 in the Npr1 promoter region containing Ets-1 binding sites.

Conclusions: Collectively, our results show that retinoic acid induces Npr1 gene transcription and expression via RAR α and Ets-1 transcription factor in target cells. The identification of retinoic acid signaling as a regulator of Npr1 gene will have important implications in hypertension and cardiovascular regulation.

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EFFECT OF PIOGLITAZONE ON PLATELET AGGREGATION IN A HEALTHY COHORT

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Purpose of Study: Peroxisome proliferator activated receptor (PPAR) agonists possibly prevent platelet aggregation. Pioglitazone is a PPAR ligand activator and an agonist of PPAR - receptors. There is controversy in literature about its antiplatelet effect; some studies show direct antiplatelet effects and others do not. Given the controversies existing in literature, we designed a study to investigate the effect of pioglitazone on platelet aggregation and lipoprotein levels in healthy young adults who would not have confounding medical disorders.

Methods Used: This prospective study was started after obtaining IRB approval. Healthy volunteers took pioglitazone for seven day period. The platelet aggregation response to adenosine diphosphate (ADP), epinephrine (EPI), collagen and arachadonic acid (AA) was measured before and seven days after the treatment. Lipoprotein levels were also measured.

Summary of Results: Twenty patients (12 males and 8 females) with a mean age 31.5 ± 7.6 years ($R=24-46$) were enrolled. Two patients did not complete the study and were excluded. The mean baseline HbA1C was 5.35 ($R=4.7-5.7$). Baseline platelet aggregation characteristic were based on mean platelet aggregation values of this healthy cohort and paired correlation statistics were used to compare mean platelet aggregation before and after pioglitazone administration. All physiologic platelet aggregation studies resulted in non-significant decreases in mean platelet aggregation values after drug treatment with pioglitazone 15mg a day. The ADP mediated platelet aggregation difference was 0.04% (p -value-0.98); AA mediated platelet aggregation difference 0.69% (p -0.92), collagen -0.29% (p -0.87) and EPI 0.93% (p -0.94). There was non-significant decrease in LDL, VLDL, total cholesterol and non-significant increase in HDL. There was no toxicity.

Conclusions: We conclude that pioglitazone does not have a direct antiplatelet effect in healthy volunteers over a seven day period. This drug needs more study in the patients with comorbid diseases to determine if it changes platelet reactivity.

Endocrinology and Metabolism

Joint Poster Session

5:00 PM

Thursday, February 25, 2010

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A LESS AGGRESSIVE METS IN PUERTO RICO THAN IN THE UNITED STATES

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Purpose of Study: Obesity linked to Diabetes Mellitus is the Epidemic of the 21Th Century. The above diseases with lipid abnormalities, plus hypertension, are clustered under "metabolic syndrome"(MetS). This syndrome is related to coronary artery disease, whose incidence varies depending on the culture. Hispanics with MetS usually shows low coronary artery disease, when compared with the U.S.A. The purpose of the study is to study why Mets is less aggressive in Puerto Rico than in the U.S.A. and its causes.

Methods Used: We studied 169 patients (P) with MetS in Puerto Rico- a U.S. Hispanic Island.

Summary of Results: 97% were diabetics Type II and 3% Type I. None showed myocardial infarction or stroke. The Ejection Fraction was reduced when compared to our normal group (49 ± 4 vs. $62 \pm 12\%$) $P<0.001$ due to diabetic cardiomyopathy. The lipid profile was normal: HDL= 48 ± 16 , LDL= 83 ± 30 . Triglycerides 166 ± 13 , Cholesterol= 166 ± 25 mg/dl. 13% showed

atrial fibrillation. No ventricular tachycardia was detected in this selected group.

Conclusions: This shows that the expression of Mets varies with culture. It is interesting that Puerto Rico, the nation more influenced by U.S. culture shows a less aggressive Mets. Less aggressive means:

1. Less coronary artery disease and strokes.
2. Less ventricular taquicardia.

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VITAMIN D DEFICIENCY AND PREECLAMPSIA IN PREGNANT WOMEN WITH TYPE 1 DIABETES MELLITUS

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Purpose of Study: Vitamin D deficiency is associated with several complications of pregnancy, including gestational diabetes and preeclampsia (PE). Women with diabetes have an increased incidence of PE. In a prospective study, we sought to determine whether vitamin D deficiency was more frequent in pregnant women with type 1 diabetes, and/or was associated with an increased risk of subsequent PE.

Methods Used: We measured maternal 25-hydroxyvitamin D levels during the first and third trimesters of pregnancy in the sera of 24 women with type 1 diabetes who subsequently developed PE (DMPE+), 23 women with type 1 diabetes but no PE (DMPE-), and 20 non-diabetic control subjects. The women were all Caucasian, and lived in Australia, Norway, and the United States.

Summary of Results: During the first trimester of pregnancy, 25-OH vitamin D levels in DMPE+ women were 17.2 ± 6.4 ng/mL (mean $\pm$ SD); in DMPE- women: 18.8 ± 7.6 ng/mL; and in controls: 22.9 ± 6.9 ng/mL. There was no difference between DMPE+ and DMPE- ($p=0.43$), but women with type 1 diabetes had significantly lower levels than non-diabetic controls (18.0 ± 6.9 vs. 22.9 ± 6.9 , $p=0.0013$). All three groups had a high prevalence of vitamin D deficiency (<30 ng/mL): 96% of DMPE+, 87% of DMPE-, and 85% of non-diabetic controls. During the third trimester, again, no significant difference was noted between DMPE+ and DMPE- women (16.6 ± 7.8 ng/mL vs. 19.5 ± 8.7 ng/mL, $p=0.22$) and the difference between all women with type 1 DM vs. non diabetes controls was less pronounced (18.1 ± 8.3 vs. 21.4 ± 8.6 ng/mL, $p=0.15$). Also at the third trimester, 96% of DMPE+, 92% of DMPE-, and 75% of controls were vitamin D deficient.

Conclusions: Vitamin D deficiency affected a large majority of pregnant women in all three study groups, and was more severe in women with Type 1 diabetes than in non-diabetic controls. There was only slight improvement over the course of the pregnancy, and although levels tended to be lower in diabetic women who later developed PE compared with those who did not, the difference did not reach significance.

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MITOCHONDRIAL DEFECTS AND INCREASED OXIDATIVE STRESS IN TISSUE FROM PRE-DIABETIC NOD MICE

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Purpose of Study: NOD mice are a model of DM1. Leukocyte infiltration around the islets of Langerhans is first seen at 5 weeks of age. We have previously reported defects in expression of mitochondrial proteins at 4 weeks (pre-pathology) in these mice. In this study we examined markers of oxidative damage to lipids and DNA, antioxidant defenses, and activity of mitochondrial complex 1, in heart tissue from NOD mice.

Methods Used: Mice from NOD and two control strains: NOR and C57BL/6 were sacrificed at 4 weeks of age ($n=10$ for each strain). The heart tissue was homogenized, and mitochondrial complex 1 activity was measured by NADH to NAD conversion. Total antioxidant capacity (TAC) was measured using a commercial kit. Lipid peroxidation was assessed by 8-isoprostane. DNA damage was assessed by 8-hydroxyl-2-deoxyguanosine (8-H-2dOG) levels. Levels of DNA repair genes: 8-oxoguanine glycosylase 1 (OGG-1), thymine-DNA glycosylase (TDG), and mammalian MutY homolog (mMYH) was measured by real time PCR.

Summary of Results: Mitochondrial complex 1 activity (COX1) was significantly elevated and antioxidant capacity (TAC) significantly reduced in the NOD group compared to both controls (see Table). Expression of two of the DNA damage repair genes (OGG-1 and TDG) were significantly reduced in NOD mice compared to C57BL/6. However, actual damage to DNA was similar in all 3 strains. Lipid peroxidation was increased in both NOD and NOR.

Conclusions: Our findings show that pre-diabetic NOD mice exhibit increased activity of mitochondrial complex 1, which may explain depletion of antioxidant defenses. Under normal conditions antioxidant defenses in NOD mice is sufficient to prevent damage to DNA and keep lipid peroxidation modestly elevated. However, at the time of initiation of autoimmunity, NOD mice are vulnerable to tissue damage if oxidative stress increases.

	C57BL/6	NOR	NOD
COX1	1.64±0.21	1.5±0.1	3.7±0.25*
TAC	12.4±2.4	16.0±2.8	3.0 ± 0.8*
8-Isoprostane	323.4±66.7	589.5±69.6*	539.0±65.4*
8-H-2 dOG-	443.7±25.6	440.8±12.4	414.9±9.6
OGG-1, mRNA	100%	119%	63%*
TDG, mRNA	100%	6.6%*	6.7%*
mMYH, mRNA	100%	93%	109%

* - $p < 0.05$ vs C57BL/6

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DEMOGRAPHIC PROXIES PREDICT DIABETES SELF-CARE BEHAVIORS ABOVE AND BEYOND HEALTH LITERACY

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Purpose of Study: A growing body of evidence has shown that compared to those with adequate literacy skills, individuals with limited literacy are more likely to have worse physical and mental health, and a shorter life expectancy. While all health literacy research has relied on surveys requiring in person administration, recent evidence suggests that demographic indicators, such as age, ethnicity, and years of schooling are highly correlated with test-based health literacy measures, and may serve as good proxies for assessing health literacy. Based on this literature, we hypothesized that health literacy would predict diabetes self-care behaviors, and that age, race, education, and income would serve as comparable predictors of these behaviors.

Methods Used: Patients with diabetes were recruited from an outpatient primary care clinic. Information gathered pertained to demographics (i.e., age, race, education, and income), and the revised Rapid Estimate of Adult Literacy in Medicine (REALM-R) was used to measure health literacy. Structural equation models tested whether health literacy predicted diabetes self-care behaviors, and whether the four demographic indicators of health literacy were better predictors of behavior after controlling for health literacy.

Summary of Results: Health literacy was not significantly predictive of diabetes self-care behaviors. Of the four hypothesized proxies of health literacy, older age ($r = 0.40$, $p < 0.001$), and more education ($r = 0.23$, $p = 0.03$) predicted self-care behaviors, but did not have significant relationships with health literacy. Income was significantly associated with health literacy ($r = 0.29$, $p < 0.01$), but was not significantly related to behaviors. Race was not significantly related to health literacy and self-care behaviors.

Conclusions: In this sample health literacy does not predict self-care behaviors. Older age and higher levels of education are independent predictors of self-care above and beyond health literacy, whereas income and race were unrelated to self-care behaviors. This suggests that age and education could serve as proxies for health literacy in predicting self-care behaviors in adults with type 2 diabetes.

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A SIMPLE DIABETES EDUCATION PROGRAM IN RURAL CLINICS IMPROVES PATIENT BEHAVIORS

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Purpose of Study: To assess the effectiveness of a simple, patient-centered, culturally-relevant, and literacy-appropriate form of diabetes education (including a diabetes guide and brief counseling).

Methods Used: All patients with type 2 diabetes seeking care in 3 FQHC's in rural North LA were eligible to participate. Clinic staff members were trained for 2 hours on implementation of the DE program. Staff members then provided each patient ($n=96$) with a diabetes guide (DG) written at the 5th grade level (and illustrated with photographs) and brief counseling. The goal of the brief counseling was to facilitate the patients' creating an individualized self-management action plan (AP). A research assistant located at LSUHSC called patients 2 weeks post-counseling for a follow-up interview assessing receipt of the DG, receipt of AP counseling, setting of an AP, recall of the AP, completion of the AP, and initiation of other self-management behaviors.

Summary of Results: Of the 69 patients reached for follow-up assessment, 99% remembered receiving the DG and 80% reported reviewing it at home. Among patients who reviewed the guide at home, more than half reported reviewing the chapters on diet (84%), exercise (65%), and insulin use (53%). Among patients reached for follow-up assessment, 72% remembered the AP they made. Two-thirds of these patients achieved their AP goal and reported maintaining the behavior, 10% achieved their goal but did not sustain the behavior, and 24% did not achieve their goal. The most frequent areas for AP's were diet (40%) and exercise (48%). Almost all patients (94%) were willing to set a new self-management AP.

Conclusions: This simple method of providing DE targeted toward patients in rural FQHCs required little staff training to produce changes in patient behaviors. This strategy of providing patient education materials and brief AP counseling may be a feasible strategy for implementing complex diabetes self-management education in rural and resource-poor settings. Patients are particularly engaged in efforts to improve their physical activity and diet behaviors.

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RECURRENT DIABETIC KETOACIDOSIS IN URBAN, INNER-CITY POPULATIONS: HEALTH, ECONOMIC, AND SOCIAL BARRIERS

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Purpose of Study: Poor compliance with therapy is a major precipitating cause for DKA in urban and indigent populations. To understand what drives poor compliance and DKA recurrence, we prospectively analyzed clinical, economic and social factors in 52 patients with multiple episodes of DKA admitted to Grady Memorial Hospital from 7/07–12/08.

Methods Used: We used questionnaires to assess potential precipitants and the PHQ-9 to screen for depression. Sixteen patients with their first DKA admission were included as controls.

Summary of Results: Patients with recurrent DKA (32M/20F, age: 40 ± 12.4 , BMI: 25.7 ± 6.4 , A1c $11.7 \pm 3\%$, $\pm$ SD) had type 1 diabetes in 79% of cases and had an average of 6 prior episodes of DKA, with 36.6% of patients having ≥ 4 episodes/year. Discontinuation of insulin was the major DKA precipitant in the recurrence and control groups (86.5% v. 87.5%, respectively, $p=NS$). Those with recurrent DKA had less concurrent medical illness, primarily infections, as compared to subjects without previous DKA (13.5 v. 25%, $p=0.272$). 19 subjects (36.5%) with recurrence had a history of mental illness, but only 42.1% were taking psychiatric (ψ) medications. Controls had a similar prevalence of mental illness but more subjects (57.1%) were on ψ medications ($p=0.665$). 71.1% v. 87.5% ($p=NS$) of patients with and without recurrent DKA were uninsured, 82.7% v. 62.5% ($p=0.164$) were unemployed, and nearly 1/3 in both groups actively used drugs or alcohol. There were no differences between groups in access to prior DM education (88% v. 75%, $p=0.352$), medical clinic (36% v. 27%, $p=0.730$) or diabetes clinic (69% v. 36%, $p=0.079$). The PHQ-9 score in those with recurrence was 10.62 ± 7.32 , suggesting that up to 78% of the cohort may suffer from depression compared to a score of 7.75 ± 6.93 in the control group ($p=NS$). Subjects that had ≥ 2 DKA episodes/year ($n=39$) compared to those with < 2 episodes of DKA ($n=29$) had significantly more substance abuse ($p=0.017$) and a higher unemployment rate ($p=0.009$).

Conclusions: The study underscores the importance of assessing socioeconomic and psychiatric factors that lead to poor adherence to treatment in patients with recurrent DKA. Addressing these factors via support groups

and education may decrease recurrence and in turn, decrease costs associated with DKA.

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IMPLEMENTING AN OBESITY COUNSELING CURRICULUM IN RESIDENCY TRAINING

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Purpose of Study: The US Preventive Services Task Force and the American Academy of Pediatrics recommends physicians screen patients for obesity and practice counseling interventions to achieve modest (4–8%) weight loss in this group. Despite these recommendations, physicians frequently fail to document obesity and counsel on weight loss. Our goal was to develop an innovative, easily disseminated curriculum that improves resident physicians' skills and confidence in weight loss counseling.

Methods Used: Beginning in July of 2009, we implemented an Obesity Counseling Curriculum based on Motivational Interviewing, a set of listening and counseling skills designed to enhance patient-centeredness and promote behavior change. The half-day session is administered monthly to Internal Medicine(IM) and Pediatric (Peds) Residents who were on outpatient rotations. The following data represents IM and Peds residents' baseline knowledge, attitudes and confidence pre-intervention.

Summary of Results: A total of 24 residents, (15 IM and 8 Peds) have completed the curriculum and completed baseline questionnaires thus far. These were distributed between PGY1 (29%), PGY2 (38%), and PGY 3 (33%) level residents. Correct responses on the 5 obesity related knowledge questions ranged from 29% to 75%. Only 43% of Internal Medicine and 25% of Pediatric Residents agreed or strongly agreed that they feel well equipped to counsel patients about weight loss. Only 43% of IM and 50% of Peds Residents agreed or strongly agreed that residency adequately equips them to address weight loss with patients. In terms of confidence, 38% of IM Residents and 58% of Peds Residents felt either very or extremely confident in assessing a patient's BMI and obesity risk, while confidence in formulating a dietary or exercise plan for weight loss with a patient ranged from 21–29% between the two groups of residents.

Conclusions: The preliminary baseline data demonstrates a gap in knowledge and confidence regarding obesity assessment and counseling. Residents do not feel well equipped by their training programs to address this issue. A curriculum that addresses this deficit may improve residents' knowledge, confidence and change attitudes in terms of weight loss counseling.

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RELATIONSHIPS OF LIPOPROTEIN SUBCLASSES BY NUCLEAR MAGNETIC RESONANCE (NMR) AND APOLIPOPROTEIN-BASED CLASSIFICATIONS

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Purpose of Study: Dyslipidemia is commonly present in diabetes and its severity is predictive of vascular complications. Lipoprotein subclasses define polydisperse particles with heterogeneity in particle size, density, and chemical composition. Methods to classify lipoproteins include NMR analysis and apolipoprotein-based lipoprotein classification. The former differentiates lipoprotein subclasses by particle diameter; the latter uses qualitative apolipoprotein composition, and so may relate more closely to metabolism. Despite the complementary nature of the two methods, there are no data describing the relationships between them, or the effects of diabetes.

Methods Used: We determined fasting lipoprotein subclass distributions using both methods in 44 healthy non-diabetic volunteers (23 male, 21 female), as well as ApoCIII in heparin-precipitable and -soluble fractions. Correlations were analyzed by stepwise regression using apolipoprotein-based lipoprotein subclasses as independent co-variables.

Summary of Results: There were significant sex differences in associations. In females, large and small VLDL and IDL correlated only with ApoCIIIHP. However, in males, large VLDL correlated with LpB, small

VLDL with ApoCIIIHP and LpB:C and IDL with LpB:C:E. Large LDL correlated, in males only, with LpB, LpAII:B:C:D:E, ApoCIIHS, and ApoCIIIHP. Small LDL particles were associated with LpAII:B:C:D:E in females and with ApoCIII-HP in males. In males, large HDL correlated with LpAI and LpAI:AI, but small HDL showed no correlations. In females, large HDL correlated with LpAI, LpAI:AI, ApoCIIHS, and ApoCIIIHP; small HDL correlated only with ApoCIIIHP.

Conclusions: Males and females exhibit marked differences in associations between lipoprotein size and apolipoprotein complement. Such effects may relate to differences in lipoprotein metabolism and mediators of disease in men and women, and may underpin known differences in associations between NMR lipoprotein subclasses and complications of diabetes in men and women.

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ONE YEAR GROWTH DATA IN MALES WITH IDIOPATHIC SHORT STATURE TREATED WITH EITHER INCRELEX OR GROWTH HORMONE

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Purpose of Study: There has been controversy over the use of Increlex in children with low IGF-1 and normal provocative Growth Hormone testing results with regards to their growth rate. Previous commentaries have suggested that Growth Hormone therapy is superior to Increlex in children with Idiopathic Short Stature(ISS). We analyzed retrospectively a group of children with similar characteristics who were treated with either Increlex or Growth Hormone(GH) for one year.

Methods Used: We analyzed 18 male children who were referred for ISS over a one-year period who had normal GH testing results with arginine and glucagon. The Increlex group had low IGF-1 values. The GH group consisted of 11 males with an avg age of 10.75 yrs who had an avg height SDS score of -2.55 before the initiation of therapy. This group had an avg peak GH level of 19.6 ng/mL and an avg IGF-1 value of 188 ng/mL. The Increlex group consisted of 7 males with an avg age of 11 yrs who had an avg height SDS score of -2.41, avg peak GH level of 22.93 ng/mL, and an avg IGF-1 level of 90.7 ng/mL. Growth velocities and height SDS scores were determined for both groups after one year of therapy controlling for Tanner stages of pubertal development.

Summary of Results: The average height SDS score for the GH group improved from -2.55 to -1.97 after one year of therapy, and exhibited an avg growth velocity of 8.22cm/yr. Within this group, those individuals in Tanner Stages I and II grew at 8.24cm/yr, Stage III grew at 6.86 cm/yr, and Stage IV grew at 9.56cm/yr. In the Increlex group, the avg height SDS score improved from -2.41 to -1.99, and the avg overall growth velocity for this group was 8.57cm/yr. Those individuals in Tanner Stages I and II grew at 8.16cm/yr, Stage III grew at 8.35cm/yr, and Stage IV grew at 9.20cm/yr.

Conclusions: Both Growth Hormone and Increlex therapy improved the average growth velocities and height SDS scores of the individuals in these two groups. However, the data analysis revealed no significant differences between the two therapies. Those individuals on Growth Hormone exhibited an average growth velocity of 8.22cm/yr as compared to those on Increlex which averaged 8.57cm/yr. These similarities can also be extended to the different Tanner Stages of development as well.

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BENEFITS OF CONTINUOUS GLUCOSE MONITORING IN TYPE 1 DIABETES MELLITUS TREATMENT: A META-ANALYSIS

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Purpose of Study: Increasing evidence shows that continuous glucose monitoring (CGM) facilitates care, reducing hemoglobin A1c (HbA1c), hypoglycemia, and hyperglycemia in type 1 diabetes mellitus (T1DM). Early CGM provided retrospective blood glucose (BG) values, but real-time (RT) CGM has been available since 2005. We conducted a systematic review and meta-analysis of randomized clinical trials (RCTs) to compare efficacy and safety of CGM versus SMBG and use of RT versus retrospective CGM in the management of T1DM.

Methods Used: MEDLINE (1966-September, 2009), the COCHRANE REGISTRY (all years), EMBASE (1980-September, 2009), and article bibliographies were searched for English language RCTs investigating CGM and/or SMBG, T1DM, and outcomes including changes in HbA1c, hypoglycemia, or hyperglycemia. Two reviewers extracted study data via a standardized instrument, rated study quality, and resolved disagreements by consensus.

Summary of Results: Seventeen RCTs met eligibility criteria and were analyzed (N=1082 patients; mean age 28.19±15.3 years; men 47.3%; Caucasian 90%; DM duration 14.73±10.19 years). We observed a significant difference between CGM and SMBG patients' HbA1c, hyperglycemia, hypoglycemia, AUC <70, and AUC>180, as shown in table 1.

Conclusions: Available evidence suggests that CGM has a positive effect on metabolic control in T1DM, with significant short and long-term reductions in HbA1c and BG derangements, and RT CGM has significantly greater effects than retrospective CGM.

TABLE 1. Glycemic control with CGM versus SMBG via RT versus retrospective BG values

Outcome	CGM v SMBG*	RT CGM†	Retrospective CGM‡	P-value
HbA1c Δ baseline to 4-8 wks	-3.47%	-4.92%	-1.58%	<0.0001*†‡
HbA1c Δ baseline to 12-16 wks	-2.43%	-2.39%	-2.43%	<0.0001*†‡
HbA1c Δ baseline to 24-26 wks	-3.49%	-3.67%	-2.39%	<0.0001*†‡
Time 71-180mg/dL (min/day)	51.47	72.53	72.53	<0.0001*†/0.01‡
Time ≥ 150 mg/dL (min/day)	-22.63	-36.07	47.12	<0.0001*†‡
Time ≥ 240 mg/dL (min/day)	-49.46	-49.46	N/A	<0.0001*†‡
Hypoglycemic(<70mg/dL) episodes/day	0.01	-0.24	0.12	<0.0001*†‡
AUC <70 (mg/dL/min)	-0.02	-0.23	0.16	0.01*/0.004†/0.30‡
AUC >180 (mg/dL/min)	-2.06	2.80	-6.39	0.003*/0.1†/0.003‡

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ETHNIC DIFFERENCES IN PRESENTATION OF PRIMARY HYPERPARATHYROIDISM

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Purpose of Study: Primary hyperparathyroidism (PHPT) is a common endocrine disorder curable only by surgical parathyroidectomy. Ethnic differences have been shown to exist in the physiological reactions to parathyroid hormone (PTH), but little is known about the ethnic differences in the clinical presentation of PHPT. We report here on clinical differences found between African-Americans, Caucasians and Hispanics with PHPT.

Methods Used: Medical records of 82 patients with PHPT who underwent parathyroidectomy at Parkland Hospital in Dallas, TX between 2003–2009 were reviewed. Data on demographic, historical, laboratory, imaging and surgical findings were collected and compared across ethnic groups.

Summary of Results: The mean age of the sample studied was 59 years old, 87% of the sample were women and the mean BMI was 30.8. The sample consisted of 38% African-Americans, 19% Caucasians and 42% Hispanic. In comparing ethnic groups, median serum calcium, PTH and urine calcium were highest in Hispanics, then African-Americans, and lowest in Caucasians (see table). However, incidence of kidney stones was significantly higher in Caucasians (56%) as compared to African-Americans (23%) and intermediate in Hispanics (37%). This lower incidence of nephrolithiasis in African-Americans is similar to what is observed in the general (non-PHPT) U.S. population. Additionally, Hispanics presented with significantly greater bone disease as shown by lower T-scores, primarily at the radius. Surgery and pathology data were similar amongst all three groups.

Median Lab Values by Race

Race	African-American	Caucasian	Hispanic
Serum Calcium (mg/dL)	11.0	10.7	11.1
Serum PTH (pg/mL)	156	134	173
Urine Calcium (mg/24h)	196	183	277

Conclusions: 1.) Ethnic differences exist in the clinical presentation of primary hyperparathyroidism.

2.) As current guidelines and clinical criteria for surgery for PHPT are largely based upon Caucasians, further research into these ethnic differences

need to be performed to assess whether the same criteria fit PHPT patients of all ethnicities.

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BIOMARKERS OF PREDIABETES IN THE LEUKOCYTE NUCLEAR PROTEOME OF NON-OBESE DIABETIC (NOD) MICE

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Purpose of Study: NOD mice develop lesions in the islets of Langerhans from about 5 weeks of age, and type 1 diabetes appears at 12 weeks of age or later. A detailed understanding of abnormalities in levels of protein expression and phosphorylation in spleen leukocyte nuclei (LN) will increase our understanding of cellular signaling mechanism associated with initiation of this autoimmune disorder.

Methods Used: Mice from NOD and two control strains: NOR and C57BL/6 were sacrificed at 4 weeks of age (n=3 independent samples were collected from each strain). Spleen LN were isolated, and 2-dimensional electrophoresis was performed on each sample. The gels were sequentially stained with a ProQ Diamond phosphoprotein stain and a Krypton (total) protein stain. Image analysis was performed to align individual protein spots and determine their relative intensity. A one-way ANOVA analysis and hierarchical clustering were performed on the data to determine differential expression of proteins and phosphorylated proteins between the three strains. Spots of interest will be excised, digested with trypsin and MALDI-TOF-TOF mass spectrometry performed on the peptide fragments to identify the protein(s) in the spots.

Summary of Results: Results from the Krypton protein stain images indicated that 83 out of 704 proteins were differentially expressed between the three strains of mice, with 17 differing between NOD and both control strains. The phosphoprotein stain images revealed 89 (from a total of 583) phosphoproteins differed between the strains and for 28 of those, NOD differed from both control strains. We are currently working on identification of these 17 proteins and 28 phosphoproteins that are differentially expressed in NOD mice compared to both control strains.

Conclusions: A comparative proteomics approach was used to successfully identify 17 protein spots and 28 phosphoprotein spots on 2-dimensional gels that were differentially expressed in NOD mice compared to both of the two control strains. Our continuing efforts should allow us to identify these differentially expressed nuclear proteins and develop new models of the early molecular events initiating the autoimmune reaction in NOD mice.

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VITAMIN D25(OH) LEVEL IN AN OBESE PEDIATRIC POPULATION DOES NOT CORRELATE WITH MARKERS OF INSULIN RESISTANCE

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Purpose of Study: Hypovitaminose (Vitamin D25(OH)) is prevalent in the pediatric population. In a recent analysis of NHANES, Vitamin D25(OH) level and markers of insulin resistance (Fasting Insulin (FI), Fasting Glucose (FG), Quicki) were positively correlated. However, in a study of obese (>95th percentile) adolescents neither FG or FI, were positively correlated although Quicki was. Therefore we attempted to clarify the Vitamin D25(OH) level relationship to insulin resistance in the obese pediatric population.

Methods Used: A retrospective analysis of the charts of patient seen in our center from April 1, 2009 to September 30, 2009, was conducted. All records were reviewed for Vitamin D25 (OH) level, FI and FG level. Homa-IR and Quicki (measures of Insulin resistance) were calculated.

Summary of Results: Vitamin D25(OH) level were identified in 172 out of 402 records. FG, FI, Homa-IR, and Quicki were NOT significantly different between the patients with hypovitaminose D25 (OH) (0-29 ng/dl) or normal Vitamin D level (≥30ng/dl). (Table 1). There was NO statistical difference in the Vitamin D25(OH) level between patients with FG < or >100mg/dl or FI < or > 17 uI/l. Furthermore within race and gender subgroups, there was NO difference in vitamin D level when stratified by Glucose or Insulin level. (Table 2)

Conclusions: In our obese pediatric population, the Vitamin D25(OH) level is not associated with markers of insulin resistance even in the at risk subgroups. Further research is needed in this specific population.

TABLE 1

Vitamin D	0-29 ng/dl	≥ 30 ng/dl	P
FG	93.30	91.75	.27
FI	39.14	29.95	.21
HOMA-IR	7.73	7.11	.34
Qwicki	.296	.303	.14

TABLE 2

	Vit D 25(OH) ng/dl all	Vit D 25(OH) ng/dl AA	Vit D 25(OH) ng/dl Females
N	172	115	111
FG (n=143)			
FG<100	23.7	21.3	22.0
FG≥100	22.5#	22.0#	22.2#
FI (n=138)			
FI<17	25.3	22.7	21.8
FI	22.0#	20.1#	21.9#
# (P=ns)			

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PLASMA MICROPARTICLES CONTAIN FUNCTIONAL MITOCHONDRIA

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Purpose of Study: Microparticles (MPs) are subcellular, membrane-encapsulated vesicles that are heterogenous in size and composition. MPs are released by most cell types and are most often measured in the plasma. They are reflective of the cell from which they are released, carrying membrane receptors and cytoplasmic contents of the parent cell. MPs have been used as diagnostic markers of various diseases. Independent labs have reported that MPs can transfer their contents, including membrane receptors, mRNAs, microRNAs, and proteins, to target cells. However, organelle transfer via an MP-dependent mechanism has never been demonstrated. To address this query, we first determined if MPs contained mitochondria. We have previously determined that there are 3 distinct MP size populations in blood. The objectives of this study were to determine if 1) MPs contain mitochondria; 2) the mitochondria contained in the MPs are functional; and 3) there is a correlation of mitochondrial content and function to MP size populations.

Methods Used: MPs, isolated from the peripheral blood of C57Bl/6 mice, were stained with MitoTracker to determine mitochondrial content, JC-1 to determine mitochondrial membrane potential, and DAPI to determine DNA/RNA content. Latex beads, ranging from 0.1–2.0 microns, were used to size the MPs. All assays were performed on the FACSaria.

Summary of Results: Mitochondria, as assessed by MitoTracker staining, were found in the 3 different size populations of MPs, but the medium and large populations contained greater than 6-fold more mitochondrial mass than the small MPs (P<0.05). Functional mitochondria were found in all MP size populations, though there was no statistical difference among the size populations. DAPI was also found to be statistically significant among the three size populations (P<0.05).

Conclusions: MPs have dual roles as diagnostic aids and mediators of cell communication and signaling. We have shown that MPs contain functional mitochondria. The amount of DAPI in the MP populations correlates to the amount of MitoTracker in those populations, indicating mtDNA may contribute to DAPI staining. These data support a novel potential role for MPs in rescue and repair of damaged cells via transfer of functional mitochondria and/or mtDNA. Supported by NIH AA07577, HL073770; LSU TRI.

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A CASE OF HYPOPITUITARISM DUE TO PITUITARY ABSCESS WITH LYMPHOCYTIC HYPOPHYSITIS

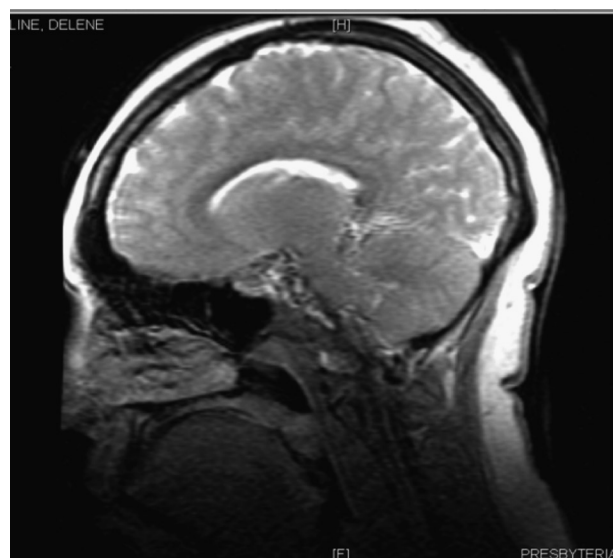
L. Mirza, M. Azar OU, Oklahoma City, OK.

Purpose of Study: n/a

Methods Used: n/a

Summary of Results: Pituitary abscess is a rare condition and few cases have been reported since 1914. Although it constitutes less than 1% of pituitary masses, it should be considered among the differential diagnoses because of its morbidity. Indeed, untreated cases of pituitary abscess are associated with increased mortality. We report here the case of a 25-year-old woman who presented with headaches, blurred vision and irregular menstrual periods for 2 months duration. Magnetic resonance imaging of the brain revealed a 1.3cm sellar/suprasellar mass impinging on the optic chiasm and resulting in bitemporal hemianopia as well as secondary hypothyroidism and adrenal insufficiency. She underwent trans-sphenoidal hypophysectomy which revealed purulent material but no definite mass. The surgical specimen was drained and cultures were obtained. The latter were positive for polymicrobial organisms, including staphylococcus aureus, streptococcus mitis, streptococcus viridans and corynebacterium species. Histopathology results were consistent with lymphocytic hypophysitis. Over the past five years, approximately 25 cases of Pituitary abscess have been reported, but none associated with lymphocytic hypophysitis. This may be the first case in the literature.

Conclusions: n/a



1.3 cm pituitary mass

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POST SURGICAL HYPOPARATHYROIDISM- IS IT TIME FOR PARATHYROID HORMONE (rhPTH)?

S. Padmanabhan, M. Azar University of Oklahoma, Oklahoma City, OK.

Case Report: Conventional treatment for post surgical hypoparathyroidism has been calcium and vitamin D analogs. We describe here two patients with iatrogenic hypoparathyroidism who were successfully treated with rhPTH.

Case No:1: A 74 yr old man underwent radical neck dissection for invasive squamous cell carcinoma. Postoperatively, he had to be readmitted several times to control his hypocalcemia on conventional therapy despite good therapeutic adherence. He was started on rhPTH at 20mcg daily which resulted in progressive discontinuation of sevelamer (used for hyperphosphatemia) and calcitriol with minimal daily doses of calcium. The follow up calcium levels remained in the low normal range. The patient eventually discontinued rhPTH injection after several months of stable calcemia due to financial constraints.

Case No:2: A 61 yr old woman underwent total thyroidectomy for goiter as a teenager. She developed pericardial calcifications as well as nephrocalcinosis and renal failure from prolonged treatment with calcium and vitamin D. She was started on rhPTH at a dose of 20mcg daily which resulted in lower daily calcium intake and discontinuation of calcitriol. Her calcium level, which was monitored closely thereafter, remained in the low normal range. She continues to tolerate the treatment several months into it.

Discussion: Over the past decade, through a series of studies, Winer et al have shown that rhPTH is effective and safe when compared to conventional therapy in terms of maintaining calcium within or below the normal range with concurrent normalization of urinary calcium. The safety of the long term rhPTH treatment in humans is of concern due to increased dose dependent osteosarcoma risk in rhPTH-treated rats. Further studies are needed to address this issue.

Conclusion: Potential targets for this novel treatment in post surgical hypoparathyroidism are patients whose calcium is difficult to maintain using conventional treatment and/or have developed complications in the form of hypercalciuria, nephrocalcinosis and renal failure. Further long term trials addressing its safety and optimal dose are awaited.

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PEDIATRIC BLOOD PRESSURE WHEEL: AN EFFICIENT SCREENING TOOL FOR PEDIATRIC BLOOD PRESSURES

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Purpose of Study: The prevalence of childhood obesity has been rapidly increasing over the years, according to a Journal of Hypertension (June 2008). This article estimates that 20% of children aged 6–11 yrs are obese and a larger percentage are overweight. Among the many co-morbidities associated with obesity, abnormally elevated BP has a dramatic impact on the quality of life of children and future impact on cardiovascular and renal disease. According to a recent publication in Pediatrics (June 2009), approximately 75% of pediatric hypertension and 90% of pediatric prehypertension goes unrecognized in the primary care setting. The reason for this finding is likely the time intensive and complicated task of calculating pediatric blood pressure norms based on gender, age, and Ht percentile. The goal of this study was to measure the recognition of abnormal BP in the pediatric outpatient setting and implement a screening tool to optimize care delivered to patients.

Methods Used: A retrospective chart review was conducted from Oct 2008–July 2009 in order to identify the prevalence and recognition of abnormal BP in the pediatric endocrine outpatient clinic. Once a baseline was established, the pediatric blood pressure screening wheel was introduced to the outpatient clinical practice in order to assess if it could improve the recognition of abnormal BP. The collection of data is currently underway and will be completed by Dec 2009.

Summary of Results: Based on data collected from the retrospective chart review approximately 35% of patients seen in the Pediatric Endocrine clinic have hypertension/prehypertension versus 7–12% of children seen in the outpatient clinical setting in the United States. Of these patients seen in clinic approximately 66%–75% of abnormal blood pressure values were unrecognized prior to the introduction on the pediatric blood pressure wheel. Preliminary data from Sept. 2009 shows that with faithful usage of this screening tool 90% of abnormal blood pressure values are identified.

Conclusions: Introduction of the pediatric blood pressure wheel as a screening tool could improve the recognition of abnormal BP in the outpatient clinical setting. This inexpensive, novel and efficient screening tool could be used easily by primary care providers and ultimately improve the quality of care delivered to all children.

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ACUTE HYPERCAPNIC RESPIRATORY FAILURE IN A PATIENT WITH THYROTOXIC HYPOKALEMIC PERIODIC PARALYSIS

O. Rad Pour, M. Rivaz, J. Fisher, S. Dagogo-Jack *University of Tennessee, Memphis, TN.*

Case Report: Introduction: Thyrotoxic hypokalemic periodic paralysis is mostly diagnosed in young Asian men with hyperthyroidism and is characterized by transient, reversible episodes of muscle weakness and hypokalemia. We report the very rare complication of involvement of respiratory muscles in this disorder.

Case Description: Initial presentation: A 26 year old Korean man with no significant past medical history presented with agitation and palpitation. Over the past several weeks he had lost 15 lbs in weight, despite increased appetite.

Physical exam: Patient was afebrile; the heart rate of 140/min, regular. Moderate thyromegaly was present. Neuro exam was WNL. Deep tendon

reflexes were brisk. Laboratory studies: TSH <0.01 mU/ml, TT4:26.5 mg/dl, TT3: 543 mg/dl, FT4:5.5 mg/dl, FT3:13.7 pg/dl; K: 3.5 mg/dl.

Diagnosis and Clinical Course: A diagnosis of severe thyrotoxicosis was made and treatment with propylthiouracil and propranolol was started as an inpatient. In the second week of hospitalization, he developed fever of 103 and reported severe weakness in all extremities. The patient was intubated 10 hours later due to shallow breathing and mental status change. The ABG's showed: PH: 7.15; PCO2:67 mmHg; PO2: 83 mmHg and HCO3:27. The serum potassium was 2.5 mmol/L. After intravenous treatment with 100 mEq KCL for 1 day, potassium increased to 3.5 mmol/L. The patient was extubated the next day; serum potassium remained stable at 4–5 mmol/L. The weakness in extremities resolved completely following potassium normalization. However, hyperpyrexia and tachycardia persisted (despite high dose PTU) over the ensuing 4 weeks. An elective subtotal thyroidectomy was performed, with prompt resolution of pyrexia and tachycardia. The patient was discharged and has remained stable one year post-discharge, requiring only supplemental thyroxine for surgical hypothyroidism.

Discussion: Very few cases of acute hypercapnic respiratory failure due to thyrotoxic hypokalemic periodic paralysis (THPP) have been reported. THPP usually involves the proximal muscles of the limbs, but on rare occasions it can affect the respiratory muscles. THPP should be kept in mind as a cause of respiratory failure in the setting of acute muscle weakness.

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IODINE INDUCED THYROTOXICOSIS IN A PATIENT WITH CORONARY ARTERY DISEASE

M. Ridella, J. Lado, K. Nugent *TTUHSC Lubbock, Lubbock, TX.*

Case Report: Iodine-containing contrast media can cause thyrotoxicosis in patients with baseline thyroid disease and this may increase morbidity and mortality in patients with coronary artery disease.

We present a 65-year old woman who developed weight loss, fatigue, tremors and heat intolerance 4 weeks after undergoing a coronary angiography and heart catheterization. Thyroid hormone levels were TSH: <0.01 and elevated FreeT4 and Free T3. TSI antibodies were positive and a thyroid uptake scan showed mildly diffuse homogeneous uptake. With the diagnosis of hyperthyroidism we started therapy with propranolol and methimazole. The patient has a daughter with hyperthyroidism.

Her physical exam revealed pulse of 70 beats per minute and rhythmic, blood pressure 180/68 mmHg, BMI 21 kg/m², no goiter, thyroid nodules, exophthalmos or pretibial myxedema were noticed, deep tendon reflexes were normal. In the following weeks the methimazole dose was decreased up to 5mg daily since the hormone levels were decreasing. Since the patient had normal TSH level before the procedure and was asymptomatic until about 3 weeks after it, our diagnosis was Iodine-induced hyperthyroidism in a patient with asymptomatic autoimmune thyroid disease.

Although iodine-containing contrast media rarely causes thyrotoxicosis in patients with no thyroid disease, the outcome is different in patients with Graves' disease, history of postpartum thyroiditis, amiodarone induced thyrotoxicosis, nontoxic nodular or diffuse goiter, autonomous nodule or patients from endemic iodine-deficiency areas, where its administration can cause thyrotoxicosis, usually after three weeks from the iodine load.

In patients with coronary artery disease thyrotoxicosis can present with angina or myocardial infarction that reflects the increase in myocardial oxygen demand in response to the increase in cardiac contractility and workload and in consequence can increase their risk of death.

For these reasons we recommend looking for indicators of thyroid disease in patients with coronary artery disease undergoing procedures with iodine-containing contrast media and close follow up to rapidly detect thyrotoxicosis. Selected patients (e.g. the elderly) may benefit from prophylactic thyrostatic therapy. Administration of iodinated contrast media is contraindicated in patients with established thyrotoxicosis.

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HEMOGLOBIN A1C: A SIMPLE COST EFFECTIVE MEASURE OF INSULIN RESISTANCE (IR) IN OBESE CHILDREN?

A. Ross, D. Preud'Homme, L. Higginbottom *University of South Alabama, Mobile, AL.*

Purpose of Study: Obesity is related to increased prevalence of IR which precedes type 2 diabetes. FI (>17 IU/ml) and/or FPG levels (>99 mg/dl) are

commonly used to diagnose IR. Oral Glucose Tolerance Tests reflect postprandial hyperglycemia but is onerous and cumbersome. HbA1c reflects 3 months of glycemia, is associated with diabetes outcome, and can be done at the point of care. HbA1c has not been validated with FPG or FI in obese children in the objective assessment of IR.

Methods Used: IRB-approved retrospective chart review of obese (BMI > 95th%) patients, ages 4-18 years old in the Pediatric Healthy Lifestyle Center from 2007-2009. Demographic, anthropometrics, HbA1c, FPG, and FI were collected. The tests cost was the actual cost billed by the hospital or by the point of care.

Summary of Results: Of 742 patients, completed data were available in 336 patients with FPG, in 361 patients with FI, and in 394 patients with HbA1c. Cohort characteristics were: average age ($\pm$ sd) is 12.4 $\pm$ 4 years old, average BMI ($\pm$ sd) is 37.1 $\pm$ 10. Using this population sample, it was observed that an HbA1c of 6% had poor sensitivity (40%) and specificity (71%) to reflect impaired fasting glucose (IFG) or FI (sensitivity: 30%, specificity: 71%), but demonstrated a negative predictive value (NPV) of 88% for IFG and a positive predictive value (PPV) of 76% for FI > 17 IU/ml. The cost of test (FG) to identify IFG > 99 mg/dl and The cost of test (FI) to identify FI > 17 IU/ml was compared with the cost of HbA1c with HbA1c of 6% being cost effective (See Table 2).

Conclusions: HbA1c of 6% is cost effective within less than optimal parameters of NPV and PPV; but it does not have the required sensitivity and specificity to replace FG or FI as a marker of IR in our population of mostly African American and male.

TABLE 1

FPG (mg/dl, average $\pm$ SD)	336 (91 $\pm$ 9)
FPG > 99mg/dl	47 (14%)
FI (IU/ml, average $\pm$ SD)	361 (38 $\pm$ 43)
FI > 17 IU/ml	272 (75%)
HbA1c (% average $\pm$ SD)	394 (6 $\pm$ 0.4)
HbA1c $\geq$ 6	117 (28%)

TABLE 2

Fasting Glucose	Cost	Fasting Insulin	Cost
Unit	\$25	Unit	\$55
Population	\$8400	Population	\$19855
Cost of test(FG) to identify IFG > 99mg/dl	\$179	Cost of test(FI) to identify FI > 17 IU/ml	\$73
Cost of test(HgA1c) to identify IFG > 99mg/dl	\$168	Cost of test(HgA1c) to identify FI > 17 IU/ml	\$29

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A CASE OF REFRACTORY HYPOTHYROIDISM

K. Schurman, N. Masri, R. Richards, D. Borne *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: A 63 year old man with a history of hypothyroidism, peptic ulcer disease, iron deficiency anemia, and diabetes mellitus was referred to the emergency department for anemia (Hct 21.9%). He denied having hematochezia, hematemesis, abdominal pain or vomiting but did have chronic constipation. An esophagogastroduodenoscopy (EGD) showed Barrett's esophagus, gastric erosions, ulcers, and hiatal hernia. Biopsy results revealed the presence of *Helicobacter pylori* for which he was treated. Two colonoscopies were attempted but were unsuccessful due to constipation. He was diagnosed with severe hypothyroidism several years ago and was placed on oral levothyroxine with no improvement in thyroid function. He never had thyroid resection or ablation in the past. He was medically compliant, including taking the medicine thirty minutes before food and his other prescribed medications. On evaluation, he had the stigmata of hypothyroidism, including cold intolerance, weight gain, constipation, and hoarseness. Laboratory studies revealed that his TSH was 78.8 UIU/ml and Free T4 was 0 ng/dl. He had a PICC line placed and was started on levothyroxine IV 150 mcg daily. Nine days later his TSH was 56.46 UIU/ml, and fourteen days later his TSH was 19.8 UIU/ml. Ten days after discharge, he was readmitted with atypical chest pain and fevers and was found to have *Bacillus sp.* bacteremia; his PICC line was removed and he was treated with

Clindamycin. He was placed back on an oral daily dose of 300 mcg levothyroxine and his TSH increased to 98.3 UIU/ml within two months. His oral regimen of levothyroxine was changed to weekly intramuscular injections of 500 mcg with repeat TSH monitoring.

Severe hypothyroidism refractory to oral levothyroxine is a rare entity. The literature demonstrates such cases either in association with thyroid ablation or with medicine noncompliance. Rarely such cases are due to malabsorption of oral levothyroxine. Hypothyroidism is associated with decreased intestinal motility which should improve gastrointestinal absorption, but it is suspected that with the patient's severe hypothyroidism he may have also had gut wall edema in his small bowel which would lead to decreased absorption of oral levothyroxine.

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EFFECT OF KETONE BODIES (B-HYDROXYBUTYRATE AND ACETOACETIC ACID) ON ACTIVATION OF HUMAN T-LYMPHOCYTES

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Purpose of Study: Human T-lymphocytes (T-cells) are unique in that in their native state they are non-responsive to insulin and do not have insulin receptors (IR). When these T-cells are activated with phytohemagglutinin they express IR, and growth factor IGF-1 and IL-2 receptors and become insulin sensitive. We have previously shown that DKA induces in vivo activation of human T-cells with emergence of IR, IGF-1 and IL-2 receptors. DKA is characterized by elevated levels of glucose, ketones, and free fatty acids. This lab has previously shown hyperglycemia-induced activation of human T-cells with de novo emergence of IR and generation of reactive oxygen species (ROS) and markers of inflammation. Similarly, this lab has also shown palmitic acid-induced activation of human T-cells with production of IR, ROS, cytokines and lipid peroxidation. However, we have not yet examined the third characteristic of DKA- elevated ketone levels and its ability to activate human T-cells. The objective of this study was to assess the in vitro effect of ketones, such as β -Hydroxybutyrate (β -OH) and acetoacetic acid (AcAt), on activation of human T-cells at various concentrations and times of incubation.

Methods Used: T-cells were isolated from the blood from normal subjects and incubated in the presence of 0, 5, and 10 mM β -OH or 0, 1, 3, and 6 mM AcAt with 5mM glucose or 30 mM glucose alone for up to 72 hours. The effect of these ketones on T-cell activation was determined by measuring the expression of CD 69, IL-2, insulin and IGF-1 receptors. Markers of oxidative stress and lipid peroxidation were determined by measuring dichlorofluorescein (DCF) and malondialdehyde (MDA), respectively.

Summary of Results: Our data show that incubation of T-cells for up to 72 hours with β -OH or AcAt does not produce a significant amount of T-cell activation as measured by CD69, IL-2, insulin, or IGF-1 receptor expression as compared to our positive control of 30 mM glucose. Levels of DCF did not increase significantly over time with any concentrations of β -OH or AcAt. Nor did any significant changes occur in the generation of MDA.

Conclusions: Our data indicate that ketones may not play significant roles in activation of T-cells and generation of ROS and lipid peroxidation as observed in patients in DKA.

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PROLACTINOMAS IN ADOLESCENT GIRLS

SE. Styers^{1,2}, K. Rettig², S. Bhowmick² *¹University of South Alabama, Mobile, AL and ²University of South Alabama, Mobile, AL.*

Case Report: Prolactinomas, though the most frequent among hormone secreting pituitary tumors, vary in prevalence with age and sex. Prevalence in adults is 100 per million in the population, but is primarily a tumor among women ages 20-50. Prolactinomas are extremely rare in the pediatric/adolescent age range. We report two cases of hyperprolactinemia in adolescent girls, caused by a functional microadenoma and a cystic macroadenoma. Both girls originally presented to medical attention secondary to amenorrhea. Both patients were found to have significantly elevated serum prolactin levels (127, 77.8 ng/mL (n=1.9-25)) with otherwise preserved pituitary function. An MRI was obtained on both patients revealing radiological evidence of microadenoma in one and macroadenoma in the other, presumed to be prolactinomas. Both patients responded well to medical therapy with a dopamine agonist (cabergoline), with a return to normal

prolactin levels (22.9, 8.6 ng/mL) and in the case of the macroadenoma, a return of menstrual cycle and an actual decrease in tumor size.

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URINARY FREE LIGHT CHAIN EXCRETION IN KIDNEY DISEASE

T. Thethi, S. Ali, P. Surampudi, J. Waddadar, P. Nagireddy, S. Japa, L. Yau, J. John-Kalarickal, E. Anumele, M. Li, V. Batuman, V. Fonseca *Tulane University Health Sciences Center, New Orleans, LA.*

Purpose of Study: Urinary polyclonal free light chains excretion is elevated in early diabetic nephropathy before GFR declines. The objective is to investigate the excretion of urinary free light chains (UFLC) in men and women, with and without DM, with a body mass index <27 or >30

Methods Used: Preliminary analysis from an ongoing cross sectional study using SPSS 14.0 for windows. Subjects were divided into 3 groups (see Table 1).

Summary of Results: Among groups I and III, there was a significant difference in free Kappa, Kappa/Cr, free Lambda and Kappa + Lambda chains, $P < 0.05$

Conclusions: Results suggest excretion of urinary polyclonal free light chains is increased in obese subjects with DM and hypertension as compared to normal controls.

Characteristics of the three groups. Values are mean + SD

	I-Healthy Controls N=10	II-Obese without DM N = 40	III- Obese with DM and HTN N = 30
Age(years)	37.0 ± 0.5	45.7 ± 11.6	57.3 ± 0
BMI	22.5 ± 2.8	38.2 ± 7.5	41.6 ± 6.9
S. Creatinine (mg/dL)	0.79 ± 0.2	0.9 ± 0.3	0.9 ± 0.9
Urine Microalbumin creatine ratio(mg/g)	9.2 ± 7.54	23.7 ± 61.6	27.2 ± 70.6
Urine Kappa (mg/L) † *	14.7 ± 11.1	34.0 ± 63.7	51.0 ± 71.8
Urine Kappa/Cr (mg/L) † *	0.01 ± 0.01	0.03 ± 0.06	0.04 ± 0.03
Urine Lambda (mg/L) †	5.8 ± 14.0	2.3 ± 3.9	8.7 ± 16.5
Urine Lambda/Cr (mg/L)	0.002 ± 0.003	0.002 ± 0.003	0.006 ± 0.013
Urine Kappa + Lambda (mg/L) †	20.4 ± 15.1	36.3 ± 66.9	59.7 ± 76.9
Urine Kappa + Lambda/Cr(mg/L) †	0.01 ± 0.01	0.02 ± 0.07	0.04 ± 0.04
Glucose (mg/dL)	74.6 ± 21.0	75.7 ± 27.8	128.5 ± 50.7
Systolic blood pressure(mmHg)	119.3 ± 13.1	124.9 ± 13.3	134.9 ± 22.5
Diastolic blood pressure(mmHg)	72.3 ± 13.6	80.4 ± 6.9	79.7 ± 10.5

† = $P < 0.05$ between groups I and III * = Trend toward significance

between groups I and II [(free Kappa, $P = 0.07$), Kappa/Cr, $P = 0.08$]

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CIRCULATING CYTOKINES PREDICT PRE-ECLAMPSIA IN TYPE 1 DIABETES MELLITUS

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Purpose of Study: The aim of the present study is to investigate whether circulating cytokines related to endothelial dysfunction, inflammatory responses, insulin resistance and factors related to atherogenesis are implicated in PE in T1DM.

Methods Used: From a prospective study of 154 pregnancies (133 with T1DM, 21 non-diabetic controls), we studied serum samples obtained early in the third trimester, prior to onset of PE, from the following study subjects: i) all 25 T1DM women who subsequently developed PE; ii) 25 age- and parity-matched T1DM women who did not develop PE, and iii) 21 age- and parity-matched non-diabetic women who did not develop PE. Cytokines were measured by ELISA and included a biomarker of inflammation (CRP), markers of endothelial cell activation (VCAM-1 and ICAM-1), and biomarkers of insulin resistance and atherogenesis including PAI-1 and tPA, the tPA:PAI-1 ratio, adiponectin, leptin, and leptin:adiponectin ratio. Any positive outcome will be re-measured using serum samples from the same subjects in the first trimester.

Summary of Results: Higher levels of leptin and ICAM-1 level were detected in T1DM who subsequently developed PE vs. those who did not. There were no significant differences in other cytokines and ratios between the two groups in the third trimester. A higher level of leptin, but not ICAM was also observed in T1DM who subsequently developed PE vs. those who did not in the first trimester.

Conclusions: Leptin and ICAM might potentially to predict PE at the early stages of pregnancy and may provide a basis to monitor therapies in pregnant women with T1DM. Confirmatory studies are necessary.

Gastroenterology and Clinical Nutrition

Joint Poster Session

5:00 PM

Thursday, February 25, 2010

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CLOSTRIDIUM DIFFICILE INFECTION MASKING ULCERATIVE COLITIS

E. Bollinger¹, J. Duet¹, J. Martinez¹, B. Lo-Blaise¹, S. Pollack², B. Ruiz³ ¹LSU-Health Science Center, New Orleans, LA; ²Tulane University, New Orleans, LA and ³LSU-Health Sciences Center, New Orleans, LA.

Case Report: A 42 year old man presented with a two week history of watery diarrhea, bloating, abdominal pain, and fevers. He also reported an unintentional fifteen pound weight loss. Initial laboratory studies showed a leukocytosis and microcytic anemia. Although initial stool evaluations were negative for Clostridium difficile toxins A and B, he was started on metronidazole for presumed infectious colitis. After 8 days of persistent diarrhea, despite antibiotics, a colonoscopy was performed, revealing severely ulcerated, inflamed, and friable mucosa from the rectum to the ascending colon with multiple areas of white exudate overlying the mucosa. A stool aspirate obtained during the colonoscopy was positive for Clostridium difficile toxin and oral vancomycin was initiated. Biopsies taken during the colonoscopy revealed severe inflammation with extensive ulceration, abundant exudates, and crypt abscesses, supporting a diagnosis of ulcerative colitis (UC) and Clostridium difficile colitis. The patient improved after therapy with oral vancomycin, IV solumedrol, and mesalamine. He was discharged on high dose oral steroids and vancomycin.

Clostridium difficile colitis can both mimic and precipitate an inflammatory bowel disease (IBD) flare. Not only do patients with IBD have a three-fold increased rate of infection with C. difficile colitis, but they also have increased length of hospitalizations, higher mortality rates, and require colectomy more frequently than the average population.

Although decreased efficacy of metronidazole has been reported, it is still the first-line agent against mild to moderate C. difficile associated diarrhea. Patients with C. difficile colitis that is severe or unresponsive to therapy with metronidazole are treated with oral vancomycin. There is little data available in the literature to provide guidance for the treatment of patients who have ulcerative colitis complicated by infection with C. difficile. This case demonstrates the difficulty of diagnosing and treating UC in the presence of severe C. difficile colitis.

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ACUTE ESOPHAGEAL NECROSIS IN END STAGE RENAL DISEASE: A CASE REPORT

I. Grover, N. Ahmad, T. Abell, W. Boone *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: Acute esophageal necrosis (AEN) also known as black esophagus and necrotizing esophagitis, secondary to its acute presentation and a characteristic, circumferential, black discoloration of the esophagus, seen only at endoscopy. AEN is a rare, relatively newly described, and usually incidental finding. The differential diagnosis includes melanosis, melanoma, and pseudomembranous esophagitis. Some data suggest that esophageal ischemia secondary to temporary reduction in blood flow plays a major role in AEN by leading to extensive esophageal necrosis. Gastric outlet obstruction has also been implicated in the pathogenesis of AEN. Most patients present with upper gastrointestinal bleeding and the diagnosis is established with upper endoscopy.

Methods Used: We report a case of a 43 year old man with End Stage Renal Disease, status post renal transplant with subsequent allograft nephrectomy and multiple episodes of allograft site abscesses. He was admitted with septicemia, and ten days later had coffee ground emesis, requiring endoscopic evaluation. Endoscopy revealed black, necrosed esophageal mucosa starting at 18cm from the incisors and progressively worsening until 40cm, where it abruptly changed to healthy-appearing mucosa at the GEJ. Eight days after the first endoscopy, a repeat procedure showed healing of the necrosed esophageal mucosa; biopsies were consistent with necrotizing esophagitis.

Summary of Results: Prompt recognition of AEN, restoration of perfusion, and timely initiation of proton pump inhibitors, and correction of the underlying disorder, are key factors in decreasing mortality.

Conclusions: Multiple comorbid conditions, including end stage renal disease, shock due to sepsis, and graft rejection may have predisposed this patient to acute esophageal necrosis. Timely intervention resulted in recovery in this case, although patient required tracheostomy, but was discharged to a long term care facility in stable condition. Most treated patients recover completely; however, without treatment mortality can reach 20 to 35 percent. Antibiotics should be considered where clinically indicated, as well as correction of the underlying disorder. The most common complications include gastrointestinal bleeding, requiring evaluation by endoscopy, and esophageal stricture, which can be treated by dilation.

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EXTREME DIRECT HYPERBILIRUBINEMIA AND LIVER FAILURE IN SICKLE CELL DISEASE

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Case Report: Intrahepatic cholestasis is an extremely rare complication of sickle cell disease. Acute liver failure is the presenting symptom. There have been fewer than 50 cases reported in the literature of this complication. Early detection and treatment with exchange transfusion is the only current treatment. Unfortunately, liver transplant is not an option for these patients. Herein we present two pediatric patients with sickle cell disease who within 2 years of each other presented to our institution with extremely high direct bilirubin and variable other symptoms of liver disease. A 17 year old boy with a history of frequent pain crisis was transferred to us with a total bilirubin of 90.7, direct bilirubin of 51.4, and an INR of 7, precluding the possibility of liver biopsy. He underwent multiple exchange transfusions and is currently in his second year of an exchange protocol with normal bilirubin levels and coagulation studies. As well, we report the case of a 14 year old boy who presented with right upper quadrant pain, total bilirubin of 43.2, direct bilirubin of 31, mildly elevated transaminases, and normal coagulation studies. He improved dramatically after only one exchange transfusion during his hospitalization. Both cases were thoroughly evaluated for other causes of liver disease and none were identified. Our experience leads us to conclude that (1) this condition may be less rare than previously thought; and (2) exchange transfusion is definitive therapy in both the acute and chronic treatment of this disease entity.

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MUCOSAL ELECTRO PHYSIOLOGIC CHANGES IN GASTROPARETIC PATIENTS AFTER TEMPORARY GASTRIC ELECTRICAL STIMULATION

B. Heindl, D. Spree, A. Kedar, C. Lahr, T. Abell *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: Many patients with gastroparesis (GP) undergo gastric electrical stimulation (GES) when drugs have not proved beneficial. Although GES has been effective in alleviating GP symptoms, its physiologic effects are not completely understood. Here we determined the electrophysiologic effects on the gastric mucosa.

Methods Used: 42 patients (35 women; 7 men; age range 17-70) treated for GP between August 2007 and March 2009, underwent Electrogastrogram (EGG) before and after temporary GES (tGES) for drug refractory GP to obtain frequency, amplitude, and their ratio (f/a). The high frequency group had an initial mucosal frequency of <3.3 cycles per minute (cpm); the low frequency group had an initial frequency of less than 3.3 cpm.

Summary of Results: Of the 42 patients, 7 had a low and 35 had a high initial mucosal frequency. Regardless of initial frequency, all mucosal frequencies moved toward a central point (5.027 cpm). The ratios for both patient groups consistently increased, though not significantly. Amplitude was not affected by stimulation.

Conclusions: With tGES, initial low mucosal frequencies at EGG increased, and high ones decreased, toward a mean value of 5.0 cpm after stimulation. Future studies are needed to determine whether or not symptom relief may be related to electrophysiologic responses.

TABLE

Patients	Initial Freq	Post-GES Freq	p value	Initial Amp	Post-GES amp	p value	Initial Ratio	Post-GES Ratio	p value
All Patients	5.42012	5.09214	0.4776	0.9014	0.7757	0.5159	18.7357	27.0731	0.1987
Low Frequency (7)	3.0957	4.9314	0.0155	0.6843	0.5157	0.6574	11.3829	23.6829	0.2602
High Frequency (35)	5.885	5.12429	0.1347	0.9449	0.8277	0.5948	20.2063	27.7511	0.3153

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PATIENT AND PROVIDER SYMPTOM AND QUALITY OF LIFE REPORTS: A COMPARISON WITH

W. Horton, A. Kedar, T. Cutts, R. Bhakta, R. Humble, D. Spree, T. Abell *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: The SF-36 (Short Form-36) is described by its developer as "a multi-purpose, short form health survey". Here we present simple, cost-effective, disease and symptom-specific assessments for use in the clinical evaluation of GI disorders using a Patient Diary (Total Symptom Score TSS). These tools are specifically designed to help identify patients with gastroparesis (GP), who often experience a range of inappropriate interventions before the disorder is accurately diagnosed. We calculated TSS index values from patient self-reports and correlated them with the patients' SF-36 values for Physical Function, Role Physical, Bodily Pain, General Health, Mental Health, Role Emotional, Social Function, and Vitality.

Methods Used: The patients included in our study (n=242 in the first component, and n=235 in the second and third components) were diagnosed with gastroparesis (idiopathic=59%, diabetic=29%, post-surgical=12%), had a mean age of 47 years, included females (79%) and males (21%), and were ethnographically distributed (82% Caucasian, 17% African American, and 1% other ethnicities). The TSS index is calculated from streamlined, quantitative, patient symptoms diaries, in which patients can record, on a Likert scale.

Summary of Results: Spearman correlation was used for the statistical analysis of all assessments. These comparisons were also used to determine the validity of symptom ratings in the Patient Diary/TSS measures for patients with gastroparesis. Significant correlation coefficients are listed in the table below.

TABLE

	Physical function	Body pain	Emotional scores	Social function	Mental health
Vomiting severity				r=-0.236 p=0.000	
Bloating severity	r = -0.202 p=0.002	r=-0.220 p=0.001	r=-0.284 p=0.000		r=-0.182 p=0.005
Bloating frequency	r = -0.188 p=0.004	r=-0.180 p=0.005	r=-0.225 p=0.001		
Epigastric pain severity	r=-0.180 p=0.006	r=-0.190 p=0.006	r=-0.194 p=0.003		
Epigastric burn severity		r=-0.200 p=0.003			
Epigastric pain frequency		r=-0.196 p=0.004		r=-0.188 p=0.005	

Conclusions: The results support the concurrent validity and utility of the Patient Diary/TSS index as a helpful PRO in the context of GP, and SF-36

values correlated especially well with the Sickness Impact profile and psychological general well-being scale. Of note for future studies, TSS ratings of vomiting correlated with baseline SF-36 values.

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GASTRIC BEZOAR MANIFESTING AS ACUTE PANCREATITIS (RAPUNZEL SYNDROME)

S. Islam, E. Islam, K. Nugent *Texas Tech Health Sciences Center, Lubbock, TX*

Purpose of Study: Patients who have gastric bezoars typically present with acute bowel obstruction and need surgical management. However, a subset of patients present with acute pancreatitis. These patients require conservative management strategies with attempted endoscopic removal of the bezoar. Our goal was to determine which patients have bezoars presenting as acute pancreatitis, disease characteristics, and possible management options.

Methods Used: We identified all cases in the English PubMed database with Mesh search terms bezoars, and/or Rapunzel syndrome, and pancreatitis.

Summary of Results: We identified 8 cases with a median age of 29 (range 15 to 59). Eighty-five percent of the patients were female. Four patients had a trichotillomania as a psychiatric co-morbidity. The initial presentation was nausea and vomiting in 4 patients, pain in 5 patients, while 4 patients had melena or occult blood in the stool. The initial median amylase was 1250 international units/liter, and all the patients had imaging consistent with acute pancreatitis. None of the patients had reported lipase levels. Imaging demonstrated that the bezoars extended into the duodenum in all patients. All were initially treated conservatively with NPO status and IV fluids. Endoscopy was initially tried in 5 patients and was only successful in removing the bezoars in 3 patients. A surgical procedure was successful in 4 patients, either as the initial treatment (n-2) or as a result of failure of endoscopy (n-2). All patients had a psychiatry referral after removal of the bezoar.

Conclusions: Patients with co-morbidity of trichotillomania may present with acute pancreatitis due to a trichobezoar (Rapunzel syndrome). It is thought that the bezoar tail extends to the ampulla of Vater, causing "irritation" and pancreatitis. The typical patient is a female with a psychiatric history of trichotillomania. The presentation is similar to acute pancreatitis, with nausea, vomiting, and an elevated amylase. Management should be initiated with endoscopy, but surgical intervention may be necessary. No matter how the bezoar is removed, all patients need psychiatric referral.

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GASTROINTESTINAL STROMAL TUMOR PRESENTING AS BACTERIAL PERITONITIS

GD. Valdez¹, J. McKinney³, RP. Byrd³, T. Roy³, RD. Smalligan² ¹*University of Washington, Seattle, WA;* ²*TTUHSC, Amarillo, TX* and ³*East Tennessee State University, Johnson City, TN.*

Case Report: A 49-year-old man was admitted with a 5-month history of intermittent abdominal pain, watery diarrhea, nausea and vomiting and increasing abdominal girth. Two weeks before admission he developed lower extremity edema, dyspnea on exertion and hematochezia and was finally admitted when he became extremely weak and short of breath. Past medical history - GERD and osteoarthritis; Social history: denied alcohol, smoking and illicit drugs. Physical exam: confused man, BP 87/60, HR 109, RR: 20, Temp 37°C, scleral icterus, no JVD, lungs-clear; heart-RRR, no murmur or gallops; abdomen-decreased bowel sounds, diffuse tenderness, no rebound, tense ascites; lower extremities-2+edema. Laboratory: WBC: 5000, neutrophils 92%, lymphocytes 7.4%, Hgb 13.9, platelets 186,000, albumin: 3.1, bilirubin 6, alk phos 189, ALT 75, AST 64, amylase 30, ascitic fluid: RBC 320, WBC 14,520, PMN: 93%; protein 2.8, glucose <20; culture grew *E. coli*. Abdominal CT: multiple intra-abdominal masses and a 14.6 × 19cm complex mass extending from the mesentery to the peritoneum. The patient developed septic shock and multi-organ failure and died 3 days later. Autopsy and histology showed the large mass to be a gastrointestinal stromal tumor of the spindle cell type.

Discussion: Gastrointestinal stromal tumors (GIST) are rare sarcomas of the GI tract with an incidence of 6–8 cases/million. Most of the cases arise from the stomach (50%), small bowel (25%) and colon (10%). Typically these tumors present with gastrointestinal bleeding, intestinal obstruction or perforation, as an abdominal mass, or as an incidental finding. Our patient had a fistula between the large mass and the intestinal tract that contributed to

the diarrhea and most likely a small perforation which led to the peritonitis and rapid deterioration. Treatment of GIST depends on the stage at the time of diagnosis, with surgery being the only curative therapy if discovered before metastasis has occurred. More than 95% of these tumors express a family of tyrosine kinases (PDGF α , KIT) hence imatinib, a tyrosine kinase inhibitor, has been used and has shown some promise in more advanced cases with 2-year survival rates of up to 70%.

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CONSERVATIVE MANAGEMENT OF EMPHYSEMATOUS GASTRITIS: REPORT OF A CASE WITH REVIEW OF LITERATURE

SR. Walvekar, J. Melancon, J. Martinez *LSU Health Sciences Center, New Orleans, LA.*

Purpose of Study: Emphysematous gastritis (EG) is a rare and a fatal condition characterized by air in the gastric wall. We describe our experience with a case of EG managed conservatively with a successful outcome along.

Methods Used: A chart review was performed and a PubMed literature search was conducted using the key word "emphysematous gastritis".

Summary of Results: Our literature search revealed only 41 reported cases of this rare condition. A 58 year old diabetic woman presented to the emergency room with severe back pain and weakness. A urinary tract infection was diagnosed. A computerized tomography (CT) scan of the abdomen obtained secondary to severe back pain revealed bilateral hydronephrosis with a distended bladder consistent with pyelonephritis of the right kidney and air in the wall of the stomach and in the intra-hepatic biliary ducts. Hemoglobin A1C was 14.1% and blood and urine cultures were negative. Endoscopy revealed large necrotic areas of gastric wall ulcerations. Gastric fluid grew *Candida albicans*. The patient was managed conservatively with flucanazole, vancomycin, piperacillin-tazobactam, and insulin. In view of stable hemodynamics and the high morbidity and mortality associated with surgery, surgical intervention was deferred. Total parenteral nutrition (TPN) for seven days with restriction of oral intake with continued conservative management resulted in a significant improvement confirmed with a repeat esophagogastroduodenoscopy. The patient was discharged tolerating a clear liquid diet without the need for surgical intervention.

Conclusion: Although, surgical intervention is recommended for of managing patients with EG.

Conclusions: Although, surgical intervention is recommended for of managing patients with EG having extensive gastric ulcerations as in our case, conservative management with appropriate antimicrobial coverage and monitored progress with serial endoscopy resulted in a successful outcome.

Health Care Research

Joint Poster Session

5:00 PM

Thursday, February 25, 2010

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POST-TRANSLATIONAL REGULATION OF P53 DURING NEPHROGENESIS

K. Aboudehen, G. Aljomah, S. Hilliard, S. Dipp, Z. Saifudeen, S. Eldahr *Tulane University, New Orleans, LA.*

Purpose of Study: p53, a tumor suppressor/transcription factor, protects the genome by promoting cell cycle arrest and differentiation or apoptosis. In response to stress, p53 is stabilized and activated via phosphorylation/acetylation which prevent its association with the ubiquitin ligase mdm2 and enhance its DNA-binding affinity. We tested the hypothesis that the p53 protein is developmentally regulated via post-translational modifications.

Methods Used: we: (1) characterized the phosphorylation and acetylation status of endogenous p53 during nephron differentiation; (2) assessed the effect of serine-to-alanine (p53-SA 15, 20, 33, 37, 392) and lysine-to-arginine (p53-6KR 320, 370, 372, 373, 381, 382) knock-in mutations on the stability and transcriptional activity of p53; and (3) evaluated the effect of varying levels of endogenous p53 on AQP-2 expression.

Summary of Results: Western blots of mouse kidney nuclear fractions showed that the ratios of phos-p53Ser-6/9/15/20/37/392 as well as acetylated p53K-372/383 to total p53 were maintained at high levels during nephrogenesis only to reach undetectable levels by adulthood. Expression of p53-S/A mutants on a p53-null background revealed that phosphorylation

of Serines is interdependent and necessary for full stability of p53 but is not essential for its nuclear localization. In comparison, p53-6K/R mutants are retained in the nucleus and thus are more stable. Transient transfection assays revealed that p53-S/A 15,20,33,37 mutants had lower transcriptional activity ($p < 0.05$), whereas p53-S/A392 retained wild-type activity. Interestingly, p53-6K/R mutants were inactive and acted as dominant-negative in p53-positive cells. To stabilize p53 *in vivo*, E12.5 kidneys were treated with the mdm2 inhibitor, Nutlin. Nutlin stunted metanephric growth and induced premature expression of AQP2, eNaC, and CAII. Similarly, collecting duct-specific deletion of mdm2 induced renal hypoplasia and enhanced AQP2 expression.

Conclusions: We conclude that: (1) early kidney development is characterized by a marked and sustained activation of p53 secondary to extensive post-translational modifications; (2) p53 acetylation is indispensable for p53 transcriptional activity, whereas p53 phosphorylation regulates p53 stability; (3) fine-tuning of p53 stability is essential for renal development.

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IN SEARCH OF A TOOL TO PREDICT INFLUENZA POSITIVITY

TE. Bell¹, RD. Smalligan¹, M. Chua¹, S. Milton¹, JR. Pierce² ¹Texas Tech University Health Sciences Center, Amarillo, TX and ²UNMHSC, Albuquerque, NM.

Purpose of Study: It has been estimated that seasonal flu is responsible for more than 100,000 hospitalizations and 36,000 deaths annually in the United States, primarily affecting patients at the extremes of age. Early detection of influenza is essential for proper management, but rapid antigen tests have low sensitivities and viral culture or RT-PCR require days to get results. Physicians typically must use non-specific clinical definitions such as "influenza like illness" (ILI) in determining treatment for patients. This study sought a simple clinical tool to identify patients most likely to be "flu-positive" based on symptoms, signs, and demographics.

Methods Used: A convenience sample of patients presenting to a university based internal medicine clinic in northwest Texas with fever ($T > 38$) and sore throat or fever and cough who agreed to the informed consent had nasal swabs taken for rapid flu antigen detection. Because of the small size of this pilot trial, no attempt was made to perform logistic regression.

Summary of Results: 34 patients who met inclusion criteria were studied. The mean age was 35.8 (range 21–71); 14 (41%) males, 20 (59%) females; 8 (23%) tested positive for influenza A or B. There was no clear correlation between flu positivity and age, gender, socioeconomic status, presence of comorbidities, temperature, or blood pressure. A trend was noted of less tachycardia in patients with negative flu tests. A heart rate less than 88 was noted to have a negative likelihood ratio of 0.2 (95% CI 0.03–1.28).

Conclusions: Although this finding did not reach statistical significance in this small pilot trial, if validated, many patients with non-specific flu-like symptoms could avoid the increased cost and risks associated with antiviral therapy by utilizing an easily obtained clinical data point. Even during an influenza epidemic, only 1/3 of patients presenting with ILI actually have influenza infection. A normal heart rate would decrease the post-test probability of influenza to less than 10% in these individuals. This study has important limitations based on small size, lack of information on medications, and the use of a rapid antigen test as a proxy for a gold standard. These findings, however, warrant additional study.

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GULF COAST INFANT SLEEP PRACTICES

F. Kency, K. Savells University of South Alabama, Mobile, AL.

Purpose of Study: Sudden Infant Death syndrome (SIDS) is one of the leading causes of infant deaths in the United States. Since the introduction of the "Back to Sleep" campaign in 1994, there has been a 43% decrease in the rate of SIDS nationwide and a 56% decrease in SIDS rate in Alabama. However, there are still many unsafe sleep practices that occur in our community such as co-sleeping, sleeping on soft surfaces, and continuation of prone positioning sleep. The first goal of this project was to quantify the number of infants who are exposed to unsafe sleep practices and to determine the factors that influence the caretaker to make these choices. Secondly, to

look at local cases of SIDS and sudden unexpected infant death (SUID) through the local medical examiner's office and determine what were the known risk factors for each case.

Methods Used: Surveys were given to parents of infants to evaluate the number of infants presently exposed to unsafe sleep practices. Case file review of 22 infants that have died from SIDS/SUID in the Mobile, Alabama area in the last three years to assess common and known risk factors between each case.

Summary of Results: Our data concluded that of the 131 patients interviewed, that 39% had infants exposed to unsafe sleep practices by means of Co-Sleeping. 96% of these families who co-slept with their infant had a crib available. And of those that did have their infants in cribs, we found that 55% allowed their children to sleep in cribs with pillows, stuffed animals, and/or soft blankets and comforters. We also found that 57% had infants exposed to unsafe sleep practices by means of allowing infants to sleep on their sides, tummies, pillows, or combinations of both. Only 12% of parents reported that a physician counseled them on safe sleep. 15 of the 22 cases reviewed from the medical examiners office were known to be co-sleeping which 7 of the 15 had another bed available for the baby.

Conclusions: Both aspects of the study showed that the majority of babies in our community are exposed to unsafe sleep practices. Many of the deaths in our area could have potentially been prevented by having the infants sleep in the supine position on a firm surface in a close proximity to a parent instead of co-sleeping. This study has shown that more education in the realm of infant safe sleep needs to be provided to our community to prevent the unnecessary deaths of infants.

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2006 ESTIMATE OF COMPUTERIZED PHYSICIAN ORDER ENTRY IN HOSPITALS THAT CARE FOR CHILDREN- IS ECONOMIES OF SCALE A FACTOR IN ADOPTION?

RJ. Teufel, A. Kazley, WT. Basco Medical University of South Carolina, Charleston, SC.

Purpose of Study: In 2003, Computerized Physician Order Entry (CPOE) was estimated to be utilized by 6% of hospitals that care for children and hospital bed size did not predict adoption. We propose to determine a newer 2006 estimate and investigate hospital characteristics associated with adoption.

Methods Used: The Healthcare Cost and Utilization Project Kids Inpatient Dataset (HCUP KID) 2006 was utilized to identify hospitals that care for children. The Healthcare Information and Management Systems Society (HIMSS) 2006 database was used to identify CPOE status (automated, contracted/installing, or not automated). Children's Specialty Hospitals and hospitals without identifiers were excluded. Hospitals not reporting status were considered not automated. Bivariate analyses (chi-square) were performed to compare CPOE adoption with hospital characteristics (children's hospital type, bed size, rural/urban teaching status, ownership/control, and region). Multivariable analyses (logistic regression) were performed to determine independent predictors of CPOE adoption. Analysis performed with SAS.

Summary of Results: 2259 hospitals were analyzed. 83.9% reported CPOE status. 13.3% were automated and 20.5% were contracted/installing CPOE. Univariate analyses suggested all hospital characteristics were associated with CPOE use. Logistic regression demonstrated the following predictors of CPOE adoption: Children's Hospitals [OR 2.6 (95%CI 1.1–6.4)] and Children's Unit in General Hospital [OR 1.9 (95%CI 1.1–3.3)] compared to non-Children's Hospitals, large [OR 2.3 (95%CI 1.6–3.2)] and medium [OR 2 (95%CI 1.4–2.8)] compared to small, urban teaching hospitals [OR 6.2 (95%CI 3.2–11.8)] and urban non-teaching [OR 2.9 (95%CI 1.7–5.1)] compared to rural, private not-for-profit [OR 2.3 (95%CI 1.1–4.5)] compared to public, Midwest [OR 2.4 (95%CI 1.5–3.7)] and Northeast [OR 2.6 (95%CI 1.7–4.2)] compared to West.

Conclusions: In 2006, 13% of hospitals that care for children adopted CPOE. This is more than double our 2003 HCUP and HIMSS estimate of 6%. As compared to 2003, larger hospitals are now more likely to adopt CPOE suggesting that Economies of Scale and the size of the hospital budget may now play a role in adoption of this costly intervention in hospitals that care for children.

Hematology and Oncology**Joint Poster Session**

5:00 PM

Thursday, February 25, 2010

139**RARE BUT FATAL: CENTRAL NERVOUS SYSTEM RELAPSE OF NON HODGKIN'S LYMPHOMA**T. Armaghany, J. Glass, F. Turturro *LSU Health Science Center, Shreveport, LA.*

Purpose of Study: Central nervous system (CNS) relapse of Non-Hodgkin's Lymphoma (NHL) has become uncommon with the use of prophylaxis treatment (TX) in high risk patients but still carries a great deal of morbidity and mortality for the effected patients (pts). Recently significant advances have taken place in treating NHL and the outcomes are even more impressive with chemoimmunotherapy. The incidence of CNS relapse is reported to be 2.8% in intermediate to high grade NLHs. CNS is one of few immune privileged organs (IPO). Malignant lymphocytes lose their capability to use the human lymphocyte antigen (HLA) in order to stimulate the full blown immune system response in the IPO. CNS prophylaxis of some high risk pts with NHL, such as lymphoblastic lymphoma and Burkitt's lymphoma, is settled but there still is controversy in the prophylactic TX of other high risk NHLs such as diffuse large B cell lymphoma.

Methods Used: We retrospectively evaluated NHL pts (N=540) treated in the last 13 years in our cancer center. We report the number of pts who were diagnosed with CNS relapse, their median overall survival, and the modalities for prophylactic and therapeutic TXs. The report will review the literature regarding the pathogenesis of CNS relapse, lymphocyte homing, the immune privileged organs, occult CNS disease and the effect of Rituximab on CNS relapse. We also review the known risk factors which may assist in deciding upon if prophylaxis treatment is warranted.

Summary of Results: Among 540 patients treated in our cancer center we had 22 patients who had CNS involvement sometime during the course of their disease. Eight pts had CNS relapse, six pts had CNS involvement at presentation, two had primary orbital, three had primary testicular and 3 had primary CNS lymphoma. The incidence of CNS relapse was 1.5%, with median overall survival = 4 months (range: 2 weeks to 14 months) and the median time to relapse = 8 months. The incidence of this outcome was lower in our pt population than described.

Conclusions: CNS relapse of NHL is rare but remains fatal despite significant advances in contemporary treatment modalities. Risk stratification is a useful tool in deciding upon which patient should have CNS prophylaxis. Our data shows the incidence of CNS relapse is lower in our patient population. The epidemiology of this finding remains a matter of investigation.

140**TREATMENT OF SCLEROMYXEDEMA WITH HIGH DOSE DEXAMETHASONE: A CASE REPORT AND REVIEW OF THE LITERATURE**NT. Averett¹, S. Elkins¹, M. Shatley² *¹University of Mississippi Medical Center, Jackson, MS and ²Belle Meade Medical, Jackson, MS.*

Case Report: Scleromyxedema is a rare disease with approximately 100 reported cases in the literature. We present a case of scleromyxedema treated with high dose dexamethasone.

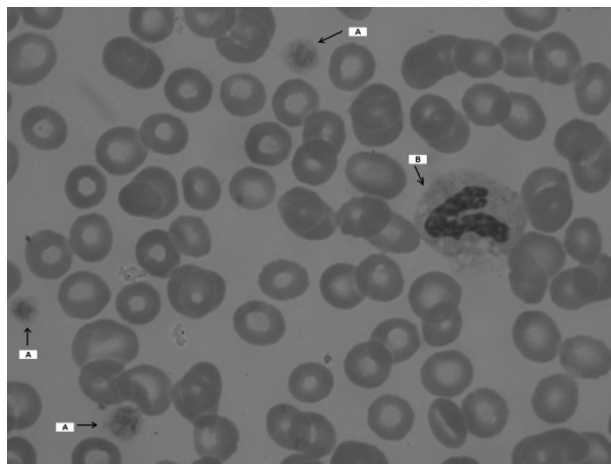
A 50-year-old White female with a history of hypertension and prolonged rash presented to an outside dermatologist. At the time of this presentation, she exhibited fine papules on her arms, chest, abdomen, back, face, and legs. Histologic sections from skin biopsy demonstrated a slightly flattened epidermis. The papillary dermis exhibited an increase in spindle cells consistent with fibroblasts. Finally, increased interstitial mucin was observed. Initial laboratory investigation revealed a monoclonal protein on SPEP. IFE revealed an IgG- κ monoclonal gammopathy. Serum free κ light chains were elevated at 45.9mg/l (3.3–19.4mg/l) and the κ/λ ratio was elevated at 5.07 (0.26–1.65). Quantitative immunoglobulins showed depression in both IgA at 53mg/dl (70–400mg/dl) and IgM at 39mg/dl (40–230mg/dl). IgG was 1250mg/dl (700–1600mg/dl) at this time. Bone marrow biopsy was performed which demonstrated a plasma cell dyscrasia with normocellular trilineage marrow. Flow cytometry detected a monotypic plasmacytic population. Several treatment options including prednisone and thalidomide were pursued but had to be discontinued secondary to side effects. Dexamethasone

was initiated at 40mg/day on days 1–4 and 9–12. Subsequent weekly dosing of the dexamethasone started on day 16 and continued with 40mg/week.

Four diagnostic criteria are used to delineate scleromyxedema from similar entities including: (1) generalized papular and sclerodermoid eruption; (2) skin biopsy with mucin deposition, fibroblast proliferation, and fibrosis; (3) monoclonal gammopathy; (4) absence of thyroid disease. Most commonly the monoclonal gammopathy is IgG- λ (80%). In conclusion, there is no standard of care for the treatment of scleromyxedema. In our patient resolution of rash and monoclonal protein have both been observed on pulse dose dexamethasone.

141**MAY-HEGGLIN ANOMALY: A RARE CAUSE OF THROMBOCYTOPENIA**SJ. Ayirookuzhi¹, A. Grosbach², GM. Mills¹ *¹LSU Health Sciences Center, Shreveport, LA and ²University of Florida College of Medicine, Gainesville, FL.*

Case Report: A 20 year old pregnant woman with a prior history of thrombocytopenia and a known congenital platelet disorder was referred to our tertiary care center for further evaluation and management of her pregnancy. Hematology-Oncology was consulted for her thrombocytopenia. An evaluation including peripheral blood smear confirmed her previously known diagnosis of May-Hegglin anomaly. The peripheral blood smear revealed numerous giant platelets, some approaching the size of red cells (arrow A) and light blue-grey basophilic inclusion bodies in the leucocytes, resembling Dohle bodies (arrow B). The platelet count in this disorder may be falsely low as the counters may not detect the giant platelets. Patients are typically discovered incidentally often at the time of a routine blood draw. They are asymptomatic and require no specific therapy. The disorder has been linked to non-muscle myosin heavy chain gene, MYH9.



Peripheral Blood Smear of a patient with May-Hegglin Anomaly

142**HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: A TALE OF THREE CASES**RR. Bamba, H. Imran, A. Rao *University of South Alabama, Mobile, AL.*

Case Report: We present three cases of hemophagocytic lymphohistiocytosis syndrome (HLH), a rare but life threatening condition of severe inflammation due to uncontrolled proliferation of activated lymphocytes and histiocytes.

Patient #1 is a 3 year old female presenting with a papular rash, fever and pancytopenia. She had hepatosplenomegaly and inguinal lymphadenopathy. Laboratory findings include elevated serum ferritin and fibrinogen and a normal triglyceride level. Viral studies were negative. Interleukin-2 (IL-2) level was markedly elevated. A bone marrow biopsy showed rare macrophages with hemophagocytoses. She received chemotherapy for 8 weeks as per HLH 2004 protocol and remains healthy without a recurrence in three years.

Patient #2 is a 16 year old male who presented with fever, chills and malaise for three weeks. Physical exam was notable for morbid obesity and

splenomegaly. Laboratory findings include pancytopenia, elevated serum ferritin, triglycerides and IL-2 levels and an absent NK function. Viral studies were negative. Bone marrow biopsy showed plasma cells with occasional large macrophages with hemophagocytoses. He received chemotherapy for 8 weeks as per HLH 2004 protocol. He remains in remission after 8 months of follow up.

Patient #3 is 6 month old male with one week history of high fever, seizures and progressive deterioration of mental status. He had anemia and leucopenia. Bone marrow biopsy showed rare cells with hemophagocytoses. After 4 weeks of chemotherapy, an improvement of his laboratory parameters was evident but no significant neurological improvement was seen. Brain biopsy showed extensive neuronal necrosis with microglial proliferation consistent with chronic encephalitis. Serum and CSF evaluation was positive for eastern equine encephalitis and west Nile viruses. He succumbed after 7 weeks of hospitalization once ventilatory support was withdrawn.

HLH may be inherited or acquired due to viral infections, collagen vascular diseases and malignancies. Diagnostic parameters as per HLH 2004 criteria are well established. Treatment with steroids and chemotherapeutic agents is directed to suppress the severe hyperinflammation and control the triggering infection.

These cases represent only a few of the many ways that HLH may present. A high index of suspicion is needed for diagnosis.

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AN UNUSUAL CASE OF PANCYTOPENIA

S. Bhatia *UF Jacksonville College of Medicine, Jacksonville, FL.*

Case Report: A 2 year-old boy presented to the ED with a 3 week history of weakness, fussiness, decreased activity, decreased appetite and pallor. He also had a 2 day history of fever, cough and runny nose. He was seen at his physician's office where he was "ill-appearing" and had mild respiratory distress.

He has a history of seasonal allergies. His medications include montelukast and a multivitamin. There were no sick contacts. He eats a normal toddler diet.

On exam, he was afebrile but pale and in mild respiratory distress requiring O2 via nasal cannula. He had poor air movement in his lung fields bilaterally. He had mild splenomegaly on his abdominal exam. He was tachycardic. His neck exam revealed shotty cervical lymph nodes. His capillary refill was about 3 seconds. His musculoskeletal exam revealed 4/5 strength in all extremities. The rest of his physical exam was within normal limits.

See table for laboratory values.

He received a pRBC transfusion and had a bone marrow biopsy the next morning. Because of his pancytopenia, he was given the presumptive diagnosis of leukemia.

The bone marrow biopsy revealed a hypercellular marrow with no blasts. Megaloblastic erythroid precursor cells, giant bands and were megakaryocytes present.

An evaluation of his macrocytosis was conducted. He had increased markers of rapid cell turnover (lactate dehydrogenase, uric acid and unconjugated bilirubin), and his reticulocyte count was much lower than expected in the face of his severe anemia. The simultaneous presence of increased markers of rapid cell turnover, low reticulocyte count, high MCV, high RDW and a hypercellular marrow indicates ineffective erythropoiesis seen with megaloblastic anemia (caused by either a deficiency of folate or vitamin B12). His B12 level was found to be low. He responded to treatment with B12. He was found to have intrinsic factor antibodies. He was diagnosed with pernicious anemia, and he continues to require B12 supplementation.

Laboratory Evaluation

	Initial	Post-Treatment
WBC	2.19 (6-17.5)	8.55 (6-17.5)
Hg	2.8 (11.2-14.3)	13.6 (11.2-14.3)
Hct	8.1 (34-40)	39.4 (34-40)
Plt	72 (150-450)	241 (150-450)
MCV	109.2 (75-87)	79 (75-87)
B12	73 (190-914)	>1500 (190-914)

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CENTRAL NERVOUS SYSTEM RHABDROID TUMORS: 10 YEARS EXPERIENCE

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Purpose of Study: CNS Rhabdoid tumors (CNS RT) are highly malignant embryonal tumors of childhood associated with poor outcomes. Median (Med) overall survival (OS) after diagnosis is 11-17 months (mos). The purpose of this review was to study presenting features, diagnostic work up, course of disease & treatment outcomes in children diagnosed with CNS RT at a regional pediatric cancer center.

Methods Used: Retrospective analysis of medical & tumor registry records from 1999-2009. Histopathology, immunohistochemistry (IHC) & cytogenetic reports were reviewed to confirm the diagnosis. Survival functions were estimated using the Kaplan-Meier method. Survival by age at diagnosis was compared using the logrank test.

Summary of Results: Nine children were diagnosed with CNS RT, 5.7% of CNS tumors (n=158). Seven were Atypical Teratoid Rhabdoid Tumors & 2 Composite Rhabdoid tumors. All were female; median age at diagnosis was 40 mos. Four were <3yrs and 5 were >3yrs of age. The most common presenting symptoms were vomiting & clumsiness followed by weakness, abnormal movements & eye deviation. Six patients (pts) had focal neurological signs & 2 had papilledema. Radiologically all tumors were large, heterogeneous, contrast enhancing with a variable presence of cystic component, necrosis, hemorrhage & calcification. The most common location was the posterior fossa (7/9). All had characteristic histopathology findings and IHC. Loss of INI1 expression was found in 7 pts & chromosome 22q abnormalities in 2 pts. 8 patients were treated with multimodality approach with surgery, chemo & radiation. Gross total resection achieved in 7/8 pts. 5/8(62%) achieved initial remission, 2/8(25%) were non responders & one patient had stable disease on treatment. Relapse or progression of disease seen in 5/8(62%). At 2 yrs from diagnosis overall mortality was 55%. Median EFS was 11 mos in all pts, it was 7 mos & 15 mos respectively in children aged <3yrs and >3yrs (p=0.052). Median OS was 9 mos in <3yrs. OS cannot be estimated in all pts and >3yrs.

Conclusions: In spite of multimodality therapy CNS RT's have poor outcomes with current therapeutic approach. Children younger than 3 years have worse prognosis. More research for targeted molecular therapy is needed for novel therapeutic strategies.

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ACQUIRED AMEGAKARYOCYTIC THROMBOCYTOPENIA: A CASE SERIES AND REVIEW OF THE LITERATURE

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Case Report: Patient 1 is a 75-year old Caucasian female who developed diffuse petechiae and was found to have a platelet count of 11 th/cmm. Bone marrow biopsy was normocellular with severe megakaryocytopenia. She had no response to prednisone and intravenous immune globulin. She was given cyclosporine and ATG. Her platelet count rose and she became transfusion independent. Her cyclosporine was discontinued and her hemogram remains normal.

Patient 2 is a 59-year old Caucasian male who was diagnosed with ITP after prolonged bleeding following excision of a nasal fold basal cell carcinoma. Bone marrow aspirate and biopsy was normocellular with no dysplastic features and markedly reduced megakaryocytes. Platelet count did not respond to prednisone and cyclosporine. He was given ATG. His hemogram improved, cyclosporine was tapered, and his platelet count remains normal.

Patient 3 is a 61 year-old Caucasian male who presented with spontaneous epistaxis. His platelet count was 4th/cmm. Bone marrow biopsy was hypocellular with severely reduced megakaryocytes and no dysplasia. He was given ATG and started on cyclosporine. His hemogram improved and he is currently on a cyclosporine taper with a platelet count of 143th/cmm.

Patient 4 is a 49 year-old African-American female who was admitted with heavy vaginal bleeding. Her initial hemogram showed a platelet count of 5th/cmm. Bone marrow aspirate and biopsy was done showing a normocellular marrow with no dysplasia and absent megakaryocytes. She was started on prednisone, cyclosporine, and an ATG infusion. Her ATG infusion was 45 days ago and she is still requiring platelet transfusions every three to four days.

Acquired amegakaryocytic thrombocytopenia is a rare hematologic disorder with markedly reduced or absent bone marrow megakaryocytes resulting in severe thrombocytopenia. The disorder appears to be a heterogeneous syndrome and is most responsive to immunosuppressive therapy. Antithymocyte globulin used in combination with cyclosporine has the

most promising results with multiple reported prolonged remissions as is seen in two of our four patients. Alemtuzumab or allogeneic bone marrow transplant can be considered for those with refractory disease.

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CASE REPORT OF GLIOMATOSIS CEREBRI

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Case Report: INTRODUCTION: Gliomatosis cerebri (GC) is a rare brain tumor characterized by the diffuse infiltration of the brain by glial cells. The 2007 WHO classification designates it as a neuroepithelial tumor, subtype Astrocytoma. It had been previously classified as neuroepithelial tumor of unknown origin. The reports in the literature often refer to the adult population; it is a rare occurrence in children. There have been a small number of case reports involving Temozolomide and its long term use.

CASE REPORT: A 16 year old male presented to the hospital with a 6 week history of headaches and sudden temporary vision loss. Headaches were in part thought to be due to depression, he had started antidepressant medication 4 days prior. The day prior to presentation he was at a concert when he became dizzy and had "black spots" in front of his eyes. He reported loss of vision approximately 3-4 minutes. Initial neurological exam was normal. Initial MRI reported as diffuse changes in the white matter and signal abnormality in the left parietal lobe. He then had brain biopsy read as anaplastic astrocytoma grade III. He presented with wide based gait w/o ataxia at home/one follow up visit 5 days after hospital discharge. Patient had this finding on one subsequent exam only. He was started on a course of radiotherapy and Temozolomide. He is currently on his cycle 7/10 of Temozolomide maintenance therapy. He has had serial MRIs that have shown to be stable from the initial MRI. Pt has not been able to wean off steroids during the course of treatment secondary to recurrent headaches. As a result of continued steroid use he has had a weight gain of approximately 80 lb weight along with acne.

Conclusions: Treatment course in the past has been radiotherapy alone, chemotherapy alone, or a combination. Surgery is not useful secondary to the diffuse nature of the tumor. Temozolomide oral alkylating agent has shown promising responses in the treatment of high grade gliomas in adults. Several case reports have shown promising data for the use of Temozolomide however larger studies will be needed in the future to determine optimal dosing and schedules. In several case reports, Temozolomide has been shown to have myelosuppression but without serious infection.

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A CASE REPORT OF ADULT T CELL LEUKEMIA

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Case Report: Adult T cell lymphoma/leukemia (ATLL) is an uncommon lymphoid neoplasm that occurs in patients infected with type I human T-lymphotropic virus, or HTLV-I. Incidence varies by populations according to the prevalence of HTLV-I. In the United States, the incidence of ATLL is approximately 0.05 cases per 100,000 population. Clinically, these patients present with skin lesions, hypercalcemia, lytic bone lesions, organomegaly, lymphadenopathy, and central nervous system involvement. The most characteristic feature is hyperlobated lymphocytes on peripheral smear, often described as "clover leaf" or "flower cells". Here we present a case of acute variant ATLL.

A 56 year old black female who presented to an outside hospital with 5 day history of dizziness, blurred vision, fever, and fatigue. There, her white blood cell count was noted to be 256, 000/cmm. She was then transferred to the University of Mississippi Medical Center. On arrival patient underwent urgent leukapheresis. Upon review of peripheral blood smear, she was noted to have "clover like cells". Her bone marrow biopsy showed similar cells as seen on peripheral smear. Based on smear and marrow findings, ATLL was suspected. HTLV-I testing returned highly positive. She was then diagnosed with ATLL, acute variant. We treated her with one cycle of multiagent chemotherapy. She also received intrathecal treatment for CNS prophylaxis, as well as, broad spectrum antibiotics and antifungals. The patient decided that she wanted to be treated near her home, so her care was transferred to another physician.

Adult T cell leukemia is a rare lymphoid neoplasm that typically presents as one of four variants, lymphomatous, chronic, smoldering, and acute. Here we present a case of acute variant ATLL. Survival is measured in months to years even with aggressive treatment. This disease has a high prevalence of CNS involvement. In addition, these patients are severely immunosuppressed. Therefore, patients must receive intrathecal treatment and aggressive antibiotic prophylaxis. ATLL is endemic to areas with high incidence of HTLV-1 infection, such as southern Japan, the Caribbean basin western Africa, and Peru. As stated earlier, the incidence in the United States is very low. At our institution only 3 or 4 cases have been seen over last 15-20 years.

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A CASE REPORT OF CHRONIC NEUTROPHILIC LEUKEMIA

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Case Report: Chronic neutrophilic leukemia is a rare malignancy which has been accepted as a distinct entity by the World Health Organization. It is characterized by mature neutrophilia, hepatomegaly, splenomegaly, elevated leukocyte alkaline phosphatase, elevated B12 levels, and hyperuricemia. There should be few circulating immature granulocytes, and bone marrow biopsy should reveal hypercellularity with granulocytic hyperplasia. Other myeloproliferative disorders must be excluded, including molecular analysis for the BCR/ABL fusion gene (Philadelphia chromosome) and JAK2 mutation. The mean age of diagnosis is 62 years and overall median survival is 30 months.

The case we present is a 71 year old black female with a history of MGUS sent for evaluation of a persistently elevated white blood cell count that was predominantly mature neutrophils. She was being treated for venous stasis ulcers when the elevated white blood cell count was noticed, and it was initially attributed to inflammation/infection from the ulcers. However, as the ulcers improved, her white blood cell count remained elevated. She was then referred to an outside hematologist who performed a bone marrow biopsy which revealed a hypercellular marrow of 70-90% and marked granulocytic hyperplasia. The myeloid:erythroid ratio was noted to be approximately 10:1. Flow cytometry revealed no diagnostic evidence of lymphoma, increased blasts, or other significant immunophenotypic abnormalities. At this point in her work-up, the patient was sent to us for further evaluation. The previous bone marrow biopsy slides were reviewed and confirmed by our hematopathologist. Molecular testing for JAK2 and FISH for t(9;22) were negative. Further laboratory tests revealed a B12 level of 1999 pg/mL and a LAP score of 223.

In diagnosing this disorder one must distinguish it from other chronic processes that have a neutrophilic component such as reactive leukocytosis, leukemoid reaction, chronic myelocytic leukemia, and other myeloproliferative disorders. Further, patients with this disease are reported to have a 20% chance of transformation to acute leukemia. Optimal treatment remains undetermined and the feasibility of determining one by a randomized, controlled trial is not likely an option.

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CHRONIC HYPOPLASTIC BONE MARROW IN A HEALTHY PATIENT WITH PARVOVIRUS B19 INFECTION

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Case Report: INTRODUCTION: The evaluation of children with cytopenias requires a broad evaluation of potential causes including inherited syndromes, chemical exposures, infections, malignant or autoimmune disorders. However, in many cases no specific etiology is found. **CASE REPORT:** A healthy African American 16-year-old boy without any underlying hemolytic disorder and with no recent medications was referred with asymptomatic neutropenia (ANC 418 × 106/L) in October 2008. Family history was remarkable for a brother with idiopathic aplastic anemia currently on treatment. Initial evaluation of antiviral antibodies (hepatitis, HIV, CMV, EBV) was negative.

In February 2009 his CBC showed mildly decreased platelets 136 × 109/L, normal hemoglobin, ANC 750 × 106/L. In the presence of mild bicytopenia and considering the family history a bone marrow biopsy was obtained. It demonstrated a decreased cellularity of 20% with decreased megakaryocytes and no abnormal infiltrate. Cytogenetic evaluation was normal. DEB test for Fanconi anemia, ANA and antineutrophil

antibodies were negative. Parvovirus IgM was negative while the IgG was suggestive of previous exposure. Patient remained asymptomatic with mild bicytopenia and a second bone marrow biopsy was obtained in July 2009. At this time cellularity was 75% with persistency of a decreased megakaryopoietic system. Parvovirus B19 DNA PCR in the bone marrow was positive with 700/ml copies detected.

DISCUSSION: Parvovirus B19 infection has been reported to be a cause of transient erythroblastopenia in patients with hemolytic disorders. The virus is directly cytotoxic to erythroid progenitor cells. Infrequently, parvovirus B19 inhibits hematopoiesis of three cell lineages and causes transient pancytopenia both in patients with hemolytic disorders or with immune deficiencies such as HIV. Our patient's clinical behavior supports the notion that parvovirus B19 can cause prolonged hematopoietic suppression in otherwise healthy patients. DNA PCR, rather than antibody titers constitutes a more reliable method of study for viral infection; furthermore, a sample from the bone marrow may be a more accurate measure of viral load. We suggest that it should be performed in patients with an otherwise unexplained hypoplastic bone marrow even in the absence of hemolytic anemia or immunosuppression.

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INCIDENCE AND PREVALENCE OF URETERAL CARCINOMA IN THE UNITED STATES: A POPULATION-BASED STUDY USING SEER DATASET 1973-2003

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Purpose of Study: To use the population-based data set to estimate the annual age-adjusted incidence rates of ureteral carcinoma histologic subtypes according to age, gender, and race.

Methods Used: Between 1973 and 2003, data of 5709 patients with ureteral carcinoma were collected by the National Cancer Center as part of the Institute Surveillance, Epidemiology, and End Results (SEER) registries. The patients represented nine different geographic areas, estimated about 10% of the population with proportional presentation of African American and Caucasian races. There were 3596 men and 2113 women including 5147 Caucasian, 183 African American, and 379 patients of other or unknown races. Only patients between the ages of 20 and 90 years were included in this study. The analysis is based on the 2000 United States Census.

Summary of Results: The overall annual age-adjusted incidence rate for ureteral carcinoma was 22.1 per million person-year. The incidence rate increases with age and peaks at 66.34 cases per million person-year, corresponding to the 75-84-year age group. There were four main types of ureteral carcinoma with the following annual incidence rates (from highest to lowest): 1) transitional cell carcinoma (5282 cases, 92.6% of the total ureteral carcinomas); 2) epithelial cell carcinomas (157 cases, 2.8%); 3) squamous cell carcinomas (138 cases, 2.4%); 4) adenomas or adenocarcinomas (48 cases, 0.9%). The incidence rates were also higher in men than women in all age groups. Likewise, Caucasians had higher incidence rate than African Americans in all ureteral carcinomas subtypes.

Conclusions: Ureteral transitional cell carcinomas are the predominant subtype of ureteral carcinomas. The annual age-adjusted incidence rate for ureteral carcinomas is highest in 75-84-year age group. Similarly, incidence rate is higher in men than women and higher in Caucasians than African Americans.

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A CASE REPORT OF A MALIGNANT MELANOMA RECURRING AS A SPERMATIC CORD LIPOMA

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Case Report: Malignant melanoma is a highly aggressive neoplasm of the skin that comprises 4% of all skin cancers but is the number one cause of mortality from skin cancer. It is estimated that about 68,720 new melanomas will be diagnosed in the United States during 2009. The incidence of melanoma has continued to rise over the years, and the overall lifetime risk of developing it across all patient populations is about 2%. Around 8,650 people in the United States are expected to die of melanoma during 2009.

A 65-year-old Caucasian male was originally diagnosed with a left lower extremity, biopsy proven malignant melanoma. He subsequently underwent a wide local excision with a negative sentinel lymph node biopsy. His melanoma

was staged as a IB lesion (T1bN0M0) secondary to a one millimeter thickness with a Clark's level of IV. He was then observed over the next four years without incident until he developed a left inguinal hernia, and a subsequent left calf vein mass that was felt to be a thrombosis. He underwent an elective hernia repair operation that revealed a large spermatic cord lipoma, and had the calf vein thrombosis excised. Pathology reports revealed the presence of malignant melanoma in both the spermatic cord lipoma and the calf vein thrombosis. The patient was then referred to our institution for management options. After undergoing metastatic workup with CT scanning and whole body PET imaging that has not shown any other evidence of disease, he is currently being treated with high dose interferon alpha therapy.

This case represents an unusual recurrence site for melanoma that has rarely been reported. A review of the literature revealed only one other case report of melanoma metastasizing to the spermatic cord. Metastatic melanoma is an aggressive disease that can disseminate widely to visceral sites as well as more unusual sites such as the skin, GI tract, and in this case the spermatic cord. It carries a very poor overall prognosis, and currently no treatment options are available that have been proven to prolong overall survival with metastatic disease.

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PERIVASCULAR EPITHELIOD CELL TUMOR: A CASE REPORT AND REVIEW OF THE LITERATURE

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Case Report: Introduction: Perivascular epithelioid cell tumors (PEComas) are rare, commonly benign tumors that have clinical significance due to their unpredictable metastatic potential and potential histologic misdiagnosis. We here in present patient with PEComa arising in the uterus with multiple, intra-abdominal masses.

Abstract: A 39 year old African American lady with a several month history of weight loss, abdominal discomfort progressing to abdominal pain and increasing abdominal girth. She had intra-abdominal masses on deep palpation that were non-tender and mobile. They were seen on CT scan and she was referred to Surgery for exploratory laparotomy and it showed 8x6x4 cms mass from the uterus, ovary, broad ligament and small intestine. On gross sectioning, it showed areas of hemorrhage & necrosis with cystic & solid components present consistent with a PEComa.

Discussion: PEComas are mesenchymal tumors composed of histologically and immunohistochemically distinctive epithelioid cells arranged in a perivascular distribution. These cells exhibit a clear eosinophilic cytoplasm and immuno reactivity with melanocytic markers. The most common site for these tumors is the uterus, present in 40% of cases. Other sites include the cervix, vagina, broad ligament, ovary, kidney, bladder, prostate, small intestine, extremities, retroperitoneum and skin.

PEComas are most seen in females and rare in males. They are classified as being benign, malignant, or with uncertain malignant potential. The criteria for malignancy include size >8cm, infiltrative growth pattern, areas of hemorrhage and coagulative necrosis, marked hypercellularity, nuclear enlargement with hyperchromasia, high mitotic activity and atypical mitotic figures. They are felt to have a vascular origin, because of the distribution around blood vessels, and a hormonal role because of the almost exclusive occurrence in females. They also have estrogen and progesterone receptor expression noted in the spindle cell component. Therapy generally involves total resection initially. Chemotherapy and/or radiation therapy has been used and reported in anecdotal fashion. Immunotherapy with IF- α has been reported most often, with varying levels of success.

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A CASE REPORT OF WIDELY METASTATIC HISTIOCYTIC SARCOMA

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Case Report: Histiocytic neoplasms constitute a group of varied and very rare hematopoietic malignancies. Of the non-Hodgkin's lymphomas, neoplasms of the histiocytes represent less than one percent, and carry with them a very poor prognosis with the patient often succumbing to their disease in less than one year. One subset of histiocytic neoplasm is the

histiocytic sarcoma, which is a proliferation of tissue macrophages. Histiocytic sarcoma is characterized by CD163 positivity and often shows a very aggressive growth pattern and resistance to most current medical interventions.

We present a case of a patient diagnosed with histiocytic sarcoma that showed an aggressive and ultimately fatal course. The patient was a 61-year-old Caucasian female who initially presented in September 2008, to an outside hospital with intractable back and left hip pain, fevers, and a 30-pound weight loss. During the workup, she was found to have a left paraspinal mass and biopsies were completed that were consistent with granulomatous disease. Her symptoms continued to worsen and she was referred to UMC for further evaluation. A CT scan revealed diffuse lymphadenopathy, a lung nodule, and multiple liver nodules. She was also found to have occult blood in her stool and underwent colonoscopy, which revealed numerous colonic masses. Biopsies revealed an infiltrate of large cells that were positive for CD163, lysozyme, CD45, and CD4 and negative for S100, HMB-45 and MART-1, all of which are consistent with histiocytic sarcoma. The patient elected to have no treatment for this malignancy aside from best supportive care and she expired just days after the diagnosis was obtained.

Of the previously presented cases of histiocytic sarcoma, the disseminated nature of disease in this patient that included involvement of multiple lymph node chains, lung, liver, gastrointestinal tract, and paraspinal muscle, is uncommon and signifies the aggressive nature of this neoplasm. There is minimal evidence that chemotherapy with a Cytosan, Vincristine, Adriamycin, and Prednisone (CHOP) type regimen may be beneficial for some of these patients.

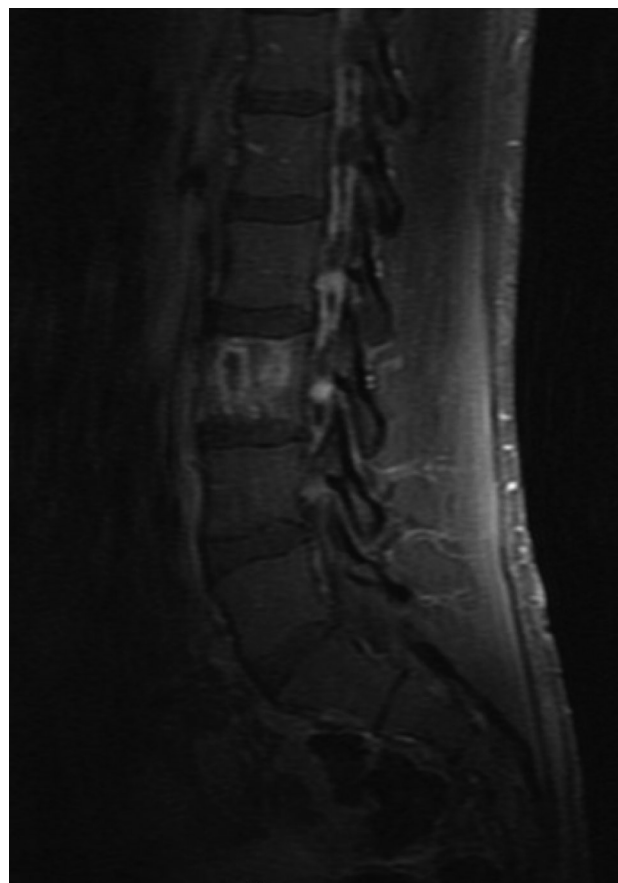


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A CHALLENGING COURSE OF HODGKIN LYMPHOMA

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Purpose of Study: Recognize the clinical presentations, differential diagnosis and challenges in diagnosing Hodgkin lymphoma.



Methods Used: 20 year-old male presented with low back pain, weight loss, fatigue, gingival bleeding, lymphadenopathy, thrombocytopenia and anemia. Lumbar MRI revealed lytic lesions but all biopsies were inconclusive with no infectious causes identified. He subsequently developed a nasopharyngeal mass, and resection revealed Hodgkin Lymphoma.

Summary of Results: Presenting symptoms of HL are vague and often mimic other illnesses. This patient demonstrated atypical features of HL.

Conclusions: A comprehensive approach is necessary in identifying underlying disease in the presence of systemic symptoms to evaluate for infectious, malignancy, and autoimmune disorders.

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TUMOR-ASSOCIATED BLOOD EOSINOPHILIA IN LARGE-CELL LUNG CANCER

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Case Report: Tumor-associated blood eosinophilia has been documented in many types of solid tumors including many types of lung malignancy, but rarely in large-cell carcinoma. Additionally, the range of eosinophilia in primary lung malignancy appears to be excessive when compared to other causes of eosinophilia such as adrenal insufficiency.

A 64 year old woman with no significant past medical history presented to the emergency department with back pain for the last three months and shortness of breath for the last four days. The patient developed a cough productive of blood-tinged sputum about six days prior to presentation. The cough was associated with pleuritic chest pain and weight loss. The patient had a 45 pack/year smoking history prior to quitting 20 years ago. Physical exam revealed decreased breath sounds and decreased vocal fremitus on the right side. Laboratory data showed a white blood cell count of 25,000/mm³ with a differential of 33% eosinophils. CXR showed total atelectasis of the right lung. CT was done and showed a large mass occupying the right hemithorax consistent with bronchogenic carcinoma. Bronchoscopy was done and the pathological data from a right main stem bronchus biopsy provided a diagnosis of large cell lung carcinoma. Metastatic disease was later discovered in the thoracic and lumbar spine, as well as the left adrenal gland which measured 3.4 × 2.0 cm. The patient was subsequently started on palliative radiation.

There have been few reports of excessive eosinophilia in confirmed large-cell lung carcinoma. The extent of eosinophilia associated with large-cell carcinoma appears to be excessive when compared to some other causes of eosinophilia such as adrenal insufficiency. One previous study noted an

eosinophilia range of 3–11% in adrenal insufficiency which contrasts the high eosinophilia ranges (26–78%) reportedly associated with large cell carcinoma. Published reports suggest that adrenal insufficiency secondary to metastatic disease would likely occur only if the cancer involved the vast majority of the normal adrenal cortex tissue in both adrenal glands. Further investigation is needed to determine if there is a prognostic value of eosinophilia associated with large cell carcinoma.

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ACUTE PROMYELOCYTIC LEUKEMIA: A SINGLE INSTITUTION EXPERIENCE

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Purpose of Study: Acute promyelocytic leukemia (APL) results from abnormal accumulation of promyelocytes in peripheral blood and bone marrow and constitutes 10–15% of adult AML. APL is characterized by the presence of PML-RAR alpha fusion transcript which results from the unique t(15;17) translocation. APL is remarkably amenable to treatment with differentiation agents such as all-trans retinoic acid (ATRA) plus an anthracycline. In addition, arsenic trioxide (ATO) plus ATRA may provide an alternative therapy especially in patients who cannot tolerate anthracyclines. The major cause of death at the time of diagnosis remains coagulopathy and with the use of ATRA the differentiation syndrome has appeared which may cause significant morbidity and mortality. The objective of the study was to examine the clinical outcome of APL patients treated at our institution.

Methods Used: This was a single institution retrospective study. Data was collected from the medical records of patients with APL between January, 2000 and December, 2008. Data on age, sex, race, WBC count at presentation were obtained. The primary objective of the study was to look at the outcome of these patients in terms of overall survival, time from induction to death and also evaluate the cause of death.

Summary of Results: Of the 20 patients with APL treated at our institution, 18 were female, 8 were African-American, with the mean age at diagnosis of 41 years (range 18 years to 83 years). Seven patients were in the high risk group (WBC count >10,000/ μ l). Two patients were treated with ATRA plus ATO and 18 received ATRA and an anthracycline based chemotherapy. One patient underwent autologous stem cell transplant following relapse. Five patients died following the start of induction with all deaths occurring from 3 days to 6 weeks from the start of induction. Three deaths were due to coagulopathy and one death was attributed to the differentiation syndrome. The remaining 15 patients were alive at the time of study and doing well.

Conclusions: Acute promyelocytic leukemia is a highly curable form of acute leukemia with deaths occurring during the initial treatment of the illness. Treatment with ATRA should be initiated at first suspicion of diagnosis. Our study suggests that these patients do extremely well if they survive the first few weeks of illness.

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MIXED PHENOTYPE ACUTE LEUKEMIA(MPAL) INITIALLY DIAGNOSED AS PRECURSOR-B LYMPHOBLASTIC LEUKEMIA

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Case Report: BACKGROUND: MPAL or biphenotypic leukemia or mixed lineage leukemia arises from a multipotent progenitor cell. Incidence ranges from less than 1% to almost 50% in various reports. Optimal treatment of MPAL probably entails high-dose chemotherapy followed by bone marrow transplantation. We describe a 6 year old male with MPAL.

CASE DESCRIPTION: A 3 year old male child presented with history of pallor and shortness of breath for several weeks. Physical examination showed cervical and inguinal lymphadenopathy, hepatosplenomegaly and scattered bruises. Blood counts showed a pancytopenia and smear revealed rare lymphoblasts. Bone marrow evaluation at an outside institution was interpreted as precursor-B lymphoblastic leukemia. Induction therapy was started as per COG protocol AALL0331. Subsequently an arterial clot secondary to Asparaginase developed leading to a gangrene and below the

knee amputation. Thereafter, therapy was switched to POG protocol 9906. After 2 years of therapy he developed a pancytopenia and a repeat marrow evaluation revealed acute leukemia. Myeloid markers (CD13, CD33, and CD15) were detected by flow cytometry in addition to precursor-B lymphoid markers (CD10, CD19, CD34, CD79a, and TdT). The child was started on AraC and Mitoxantrone therapy for AML and achieved remission which was consolidated by a matched unrelated bone marrow transplantation. He is currently in remission three months following transplantation.

DISCUSSION: This case is an example of transformation of ALL to MPAL. Alternatively, the leukemia was MPAL, but was initially mistaken as ALL. The flow cytometric findings enabled us to correctly assign the B/myeloid lineage of the leukemia and an appropriate treatment plan. While the current World Health Organization classification standardized diagnostic criteria for MPAL, the diagnosis of MPAL in the past was not reliable, as documented in this case.

CONCLUSION: MPAL is one of the childhood leukemias that clinicians and pathologists need to be aware of. Early identification and treatment will reduce morbidity in these patients.

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PANCREATIC LYMPHOMA

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Case Report: MP is a 46-year-old man who presented with complaints of right upper quadrant pain radiating to both the epigastrium and to the back, associated with nausea and vomiting $\times$ 1 month. 25 lb weight loss over the past month, no any fevers, chills or night sweats. Medical history is significant for untreated hepatitis C. He has no drug allergies nor is he on any medications at home. He has a 30pk-yr history of tobacco, drinks a 6pack of beer per day for the past 20 years. Occasional marijuana use, but has never used IV drugs.

On Physical examination he has a temperature of 96.4deg F, a pulse of 48 beats/min, respirations are 18 breaths/min and blood pressure is 126/85 mmHg. He is thin and cachectic in appearance, sclera are nonicteric, no cervical, superclavicular, axillary or inguinal lymphadenopathy. The rest of his exam was normal.

Labs reveal Hepatitis C AB positive, Ca19-9: 15, HIV negative, LDH 220, Urate 4.1, Amylase 95, lipase 81, PT 11, PTT 33.4, AST 126,ALT 132, alkaline phosphatase 375, hgb 11, WBC 3.9, platelets 232.

CT of the chest, abdomen and pelvis reveal a large heterogeneous enhancing predominately hypodense mass in the central abdomen with the epicenter in the pancreas measuring 7.5cm $\times$ 14.0 cm. No definitive hepatic masses. There was a 1.2 $\times$ 1.7 cm noncalcified nodule in the superior segment right lower lobe of the lung.

Biopsy of the pancreas mass and the lung nodule revealed a large B-Cell lymphoma. CSF studies and a bone marrow biopsy were without involvement of lymphoma. Biopsy of the lung nodule was consistent with a large B-Cell lymphoma.

Mr. MP completed 8 cycles of R-CHOP with no delays or dose reductions. CT performed at the end of therapy reveals that the mass in the pancreas is markedly diminished in size measuring 3.2 cm $\times$ 2.4 cm. Pet scan performed at the same time reveals no evidence of active disease. Mr. MP's abdominal pain, nausea and vomiting have resolved. He has regained his appetite and has gained weight.

Primary pancreatic lymphoma is a rare cancer of the pancreas that can possibly be cured without surgical intervention. Chemotherapy and radiotherapy are a good treatment option which can produce both good responses and improved quality of life.

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RETROSPECTIVE STUDY OF THE ASSOCIATION BETWEEN RED BLOOD CELL DISTRIBUTION WIDTH (RDW) AND OTHER LABORATORY PARAMETERS IN ANEMIC ADULTS

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Purpose of Study: RDW has been utilized for many years in the differential diagnosis of anemia. Recent studies have reported that RDW varies with renal function and with markers of inflammation. However, these reports were based on studies of large populations of unselected outpatients, many of whom were hematologically normal. This study was performed to examine

whether these described associations are present in a more restricted patient subset.

Methods Used: A de-identified database of 32 anemic adult inpatients (17 male/15 female, 27 Caucasian) who had undergone diagnostic bone marrow examination as part of an earlier study was examined.

Summary of Results: RDW values for 26/32 patients were in the highest quintile observed in the National Health and Nutrition Examination Survey (RDW > 13.8%). Significant differences between patients in the highest quintile and other patients were observed for hemoglobin concentration (9.9 g/dL vs. 11.6 g/dL, $p = 0.01$), serum soluble transferrin receptor (sTfR) (30.3 nM vs. 16.7 nM, $p = 0.02$), and serum interleukin (IL)-1 (1.6 pg/mL vs. 0.3 pg/mL, $p = 0.03$). No other significant differences were observed in other automated hematologic markers, in biochemical indicators of iron status, renal function, or inflammation, or in marrow aspirate iron score. When the correlation between RDW and the other parameters studied was evaluated, the only statistically significant correlations found were with C-reactive protein (CRP) ($r = -0.49$, $p = 0.009$) and sTfR ($r = 0.53$, $p = 0.002$). The significance of the correlation between sTfR and RDW was independent of other indicators of iron status, CRP, and serum IL-1. In contrast, the significance of the correlation between CRP and RDW was dependent on variation in sTfR and serum ferritin concentrations. In this group of patients with who generally had either high-normal or high RDW values, CRP and RDW were inversely correlated.

Conclusions: Associations between RDW and other laboratory or clinical parameters observed in unselected patient populations may not be applicable to complex anemic inpatients. The association between sTfR concentration and RDW appears to be independent of the relationship between sTfR concentration and patient iron status.

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MULTIPLE MYELOMA AND OTHER MALIGNANT NEOPLASMS, EXPERIENCE OF THE FEIST-WEILLER CANCER CENTER

B. Nair, Z. Abbas, C. Guedry, J. McLarty, J. Colelingam, D. Veillon, MN. Lowery, G. Mills, F. Turturro, J. Glass, R. Munker *LSU Hsc, Shreveport, LA.*

Purpose of Study: Review on association of other cancers before and after Diagnosis (Dx) of Multiple Myeloma (MM) from a large university medical center that treats patients from 59 of Louisiana's 64 parishes.

Methods Used: We obtained permission from the Institutional Review Board and performed a retrospective case review of all patients with the Dx of MM at the Feist Weiller Cancer Center (FWCC) at LSUHSC in Shreveport from 2000 to 2009. The cancer history, family history, the ethnicity and the treatments pre and post dx of MM were reviewed. The median age was 60 years and 99 patients were female and 81 male. In 180 charts, complete follow-up was available.

Summary of Results: Among these patients with MM, 23 associated cases of cancer were found (12.7%). Fifteen cases of cancer were diagnosed before the Dx of MM (8.3%) and 8 cases after the Dx of MM (4.4%). Fourteen such patients were female and 9 male. The number of patients who received chemotherapy, no chemotherapy, and autologous stem cell transplantation (ASCT) were 16, 7 and 2 respectively. Interestingly more than one malignancy was found in 4 patients (2.2%) of which had solid tumors. The types of malignancies associated with MM include breast cancer (5), prostate cancer (3), lung cancer (2), colorectal cancer (3), head and neck cancer (2), renal cell carcinoma (2), acute myelogenous leukemia (2, both post ASCT), cervical carcinoma (2), and 1 case each of myelodysplastic syndrome, ovarian, uterine and esophageal cancer.

Conclusions: Our preliminary data report the possible association of MM with other malignant tumors either before or after the Dx of MM. We plan to analyze risk factors for SMN and compare our data with registry data to investigate if SMNs are statistically increased (coincidence versus causality). With the longer survival after the Dx of MM our study is especially important to determine if the new treatment modalities and drugs have a long-term risk of second cancer.

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THROMBOTIC THROMBOCYTOPENIC PURPURA-HEMOLYTIC UREMIC SYNDROME IN POSTPARTUM PATIENTS

A. Njoku, B. Barker, T. Thayalakulasirgam *LSU-Health Science Center, New Orleans, LA.*

Case Report: A pregnant 17 year old African American women, following delivery via spontaneous vaginal delivery, was found to have elevated blood pressures. A diagnosis of pre-eclampsia was established, she was treated with nifedipine, and discharged. The patient returned to the hospital 4 days later complaining of right upper quadrant abdominal pain. The patient had two episodes of nausea and vomiting. Vital signs revealed a febrile, hypertensive, and tachycardic patient. Physical examination findings included right upper quadrant pain, bilateral CVA tenderness, and bibasilar crackles. The patient became anuric. Her platelet count decreased, creatinine increased, liver enzymes moderately increased and her LDH was markedly elevated. Schistocytes were noted on peripheral smear, suggesting a diagnosis of microangiopathic hemolytic anemia. Coombs test was negative. Prothrombin and partial thromboplastin time and fibrinogen level were normal. Urinalysis showed bloody urine, proteinuria and a red blood cell count that was too numerous for quantitation. ADAMTS 13 was 70. (Normal >67). A diagnosis of Thrombotic Thrombocytopenic Purpura-Hemolytic Uremic syndrome (TTP-HUS) was made based on the two major features, Coombs negative microangiopathic hemolytic anemia and thrombocytopenia and two minor features, fever and renal dysfunction. Her platelet count continued to decrease and urine output diminished. The patient became markedly anemic and required transfusion. Plasmapheresis and hemodialysis were initiated. The platelet count responded well to Plasmapheresis with a subsequent decrease in LDH levels and resolution of anuria. The patient continued on plasmapheresis until her LDH normalized and hemodialysis was continued until renal function improved.

TTP-HUS in postpartum patients is a rare disorder with occasional fatal outcomes. TTP-HUS causes reduced blood flow with resultant abnormalities in multiple organs secondary to the development of microscopic blood clots. The hallmark includes microangiopathic hemolytic anemia and thrombocytopenia which are the major diagnostic criteria. Postpartum patients who have recovered from an episode of TTP-HUS are more likely to suffer another episode and subsequent pregnancy is strongly discouraged.

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TREATMENT OF SEVERE ANEMIA USING A MASSIVE TRANSFUSION PROTOCOL

M. Salassi, N. Giambrone *LSU Health Sciences Center, New Orleans, LA.*

Case Report: In the setting of severe anemia, a massive transfusion protocol can be not only life-saving, but can also improve morbidity and shorten length of hospital stay.

A 45 year old women presented to the emergency department (ED) with severe symptomatic anemia (hemoglobin 1.9 g/dl). She had complaints of decreased appetite for the past 5 weeks with an associated weight loss. She also reported nausea, vomiting, dyspnea on exertion, palpitations, chest pain, and generalized weakness for 2 weeks. She noted a history of menorrhagia with passage of blood clots requiring 24 pads per cycle during the last 4 years. She stated her cycles were regular lasting 7 days, and occurring, every 28 days. She reportedly ate ice daily for 2 years. She was tachycardic with a pulse of 112 and became increasingly lethargic in the ED; she was electively intubated in order to protect her airway. On physical exam an S4, and a grade III/VI systolic ejection murmur were appreciated. She had hepatomegaly, and conjunctival pallor. On pelvic exam, there was sanguinopurulent fluid in the vaginal canal. Frank pus drained from the left wall of the vagina on examination with the speculum. On bimanual exam no masses were appreciated and her cervical os was ~ 1cm dilated. The massive transfusion protocol was initiated in the ED. She received 4 units of packed red blood cells alternating with 3 units of fresh frozen plasma. Her lactate level improved from 18.9 U/L to 1.4 U/L after the above transfusions. She was admitted to the ICU and within 36 hours was successfully extubated and transferred to the floor. Further evaluation showed that the cause of her anemia was consistent with Iron deficiency.

This case illustrates the benefits of instituting a massive transfusion protocol without delay in the setting of severe anemia. The aim of a massive transfusion protocol is to rapidly and effectively restore adequate blood volume and to maintain blood composition within safe limits with regard to oxygen carrying capacity and hemostasis. The patient's short resuscitation period was supported by a rapid response in her lab values with reversal of lactic acidosis and improvement in cardiac function shortly after initiation of a massive transfusion protocol.

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BILATERAL RENAL LYMPHOMA: CASE REPORT AND REVIEW OF LITERATUREA. Silva, J. Phillips, J. Cole *Ochsner Clinic, New Orleans, LA.*

Case Report: INTRODUCTION: Diffuse large B-cell lymphoma (DLBCL) account for 60% of all non-Hodgkin lymphomas. In 40% of the cases it also affects an extra-nodal organ, most frequently within the gastrointestinal tract. Renal involvement of lymphoma is seen in less than 1% of all cases, and usually requires renal replacement therapy. Treatment of the lymphoma is difficult due to dose delivery of drugs while on dialysis and side effects. Life expectancy is usually short, with most patients experiencing recurrence shortly after.

CASE REPORT: A 30 year-old African American man presented to the emergency room complaining of fatigue, abdominal discomfort, nausea and vomiting for 3 months. On initial evaluation he was found to be anemic with hemoglobin of 7.3g/dl and a normal white blood cell and platelet count. His creatinine was also elevated at 9.1mg/dl. The liver function was normal as well as the electrolytes. His lactate dehydrogenase (LDH) was also elevated at 541 U/L. CT scan demonstrated bilateral enlargement of the kidneys, each measuring 11.6cm and 17.9cm. The spleen also was enlarged, measuring 17cm with a heterogeneous appearance. The kidneys were biopsied and showed diffuse infiltration by B-cell lymphoma. Due to the anemia, an upper endoscopy was performed and showed areas of erosions that were biopsied and also demonstrated infiltration of diffuse large B-cell lymphoma (DLBCL). Bone marrow biopsy was negative. The patient was started on hemodialysis and chemotherapy with R-CHOP (Rituximab, cyclophosphamide, adriamycin, vincristine and prednisone) at full dose. After a total of 6 cycles patient had a complete response, with a decrease in the size of the kidneys to 7.1cm and 8.2cm. On PET scan there were no areas of hypermetabolic activity, but the kidneys appeared to be functional with normal excretion of contrast. The spleen measured 9cm. At the end of the treatment, his creatinine was 2.2mg/dl and he was taken of hemodialysis.

DISCUSSION: Diffuse large B-cell lymphoma is the most common subtype of lymphoma. Renal involvement is seen rarely and often life-threatening. We presented a case of bilateral renal involvement that was treated with full dose chemotherapy while on hemodialysis without any major complication. Complete response was achieved with significant improvement of the renal function.

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RECURRENT, TRANSFORMED NON-HODGKIN'S LYMPHOMA PRESENTING AS CHIASMAL SYNDROME WITH HYPERPROLACTINEMIA AND HYPOPITUITARISMAL. Sumrall, V. Herrin *University MS Medical Center, Jackson, MS.*

Case Report: Non-Hodgkin's Lymphoma (NHL) is a group of disorders comprised of malignant proliferation of lymphocytes. Within this group, both low and high grade variants are seen. Because this group of disorders affects lymphocytes, it may affect any organ of the body.

A 69-year-old white female with past medical history of follicular cell lymphoma presented to her local physician with new complaints of vision loss, nausea, and headaches in November 2007. Evaluation yielded the presence of an enhancing mass in the sella, extending into the suprasellar cistern and compressing the optic chiasm. The lesion measured 2.1 cm × 2.8 cm in maximum diameter. Serological evaluation for activity of the tumor yielded elevated levels of prolactin and insulin-like growth factor-1 and suppressed adrenocorticotrophic hormone, cortisol, follicle-stimulating hormone, and thyroid-stimulating hormone.

After excision, pathological examination of the tumor revealed a diffuse large B cell lymphoma. CT scans for staging revealed hepatomegaly with a hypodensity in the left lobe of the liver. Nodular thickening in the fundus of the stomach was seen also, most consistent with lymphomatous involvement. Bone marrow aspirate showed hypocellular marrow with no evidence of lymphoma.

Within two weeks of her diagnosis, she was started on treatment with ProMACE- CytaBOM. She tolerated this cycle well and was discharged home. She returned to clinic for chemotherapy, but ultimately became too ill for treatment. Hospice care was initiated, and the patient died shortly thereafter.

Non-Hodgkin's lymphoma (NHL) affecting the pituitary occurs as a primary CNS tumor or, less commonly, as spread from a concurrent systemic

lymphoma. This is usually observed in immunocompromised patients such as those with HIV. The total number of pituitary lymphoma cases in the English language literature approaches 30. Of those, 15 cases of secondary sellar lesions are present, of which 12 were NHL. This case represents the first case of recurrent, transformed NHL as chiasmal syndrome with hyperprolactinemia and hypopituitarism in the American medical literature.

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SUPPRESSION FOR THE SUPPRESSED: APLASTIC ANEMIA WITHOUT A SIBLING DONOR MATCHSC. Thigpen, C. Bigelow, S. Elkins *University of Mississippi, Jackson, MS.*

Case Report: Aplastic anemia is a rare hematologic condition with only 3 to 6 cases per million people in the United States per year. Mortality is near 70% at one year without treatment, but outcomes are dramatically improved in younger individuals with matched sibling stem cell transplant and are improved to a lesser extent with immunosuppressive therapy. Prognosis hinges on the age of the patient and the severity of aplasia.

A 17-year-old African-American woman with several months of heavy menstrual periods and frontal headaches underwent wisdom tooth extraction by her local dentist. After four days of significant maxillary pain and the expected amount of oozing of blood from her gums, she had a syncopal episode at home. She presented to a local emergency room and was found to have a hemoglobin of 2.9 g/dL, a white blood cell count of 2,000 with an absolute neutrophil count of 667, and a platelet count of 3,000. The patient was transferred to our tertiary care center where she underwent bone marrow biopsy and was found to have a markedly hypocellular marrow consistent with aplastic anemia. There was no history of chemical exposure or drug ingestion; and reflexive ANA, HIV testing, and hepatitis panel were negative. Transfusions were minimized, and the patient's lone sibling underwent HLA typing with the hope that he could be the donor for stem cell transplant. He, however, was not a match. The patient subsequently received anti-thymocyte globulin (ATG) and cyclosporine immunosuppressive therapy and tolerated it well other than a mild febrile reaction to the initial ATG infusion. Over the first month of follow-up since hospitalization, the patient remains platelet and red cell transfusion dependent.

This case highlights the management strategy for aplastic anemia in a young individual, with immediate matched sibling stem cell transplant being the first option in patients under the age of 40. In the absence of a sibling match, early immunosuppressive therapy is the next best option, with the possibility of stem cell transplant later if the response to immunosuppressive therapy is poor and a matched unrelated donor can be identified.

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ACQUIRED FACTOR IX INHIBITOR AND SUBSEQUENT RESOLUTION WITH IMMUNOTHERAPY IN A CHILD WITH ACQUIRED IMMUNODEFICIENCY SYNDROMEJ. Toler¹, CA. Morrison², G. Hescok¹, T. Singleton², RV. Gardner², C. Leissinger³, MC. Velez² ¹Louisiana State University Health Sciences Center and Children's Hospital of New Orleans, New Orleans, LA; ²Louisiana State University Health Sciences Center and Children's Hospital of New Orleans, New Orleans, LA and ³Tulane University School of Medicine, New Orleans, LA.

Purpose of Study: The development of inhibitors against coagulation factors is rare within the general population and is reported even more infrequently among pediatric patients. Factor IX inhibitors occur almost exclusively within the hemophilia B population. We present a 17 month old female with Acquired Immunodeficiency Syndrome (AIDS) and no history of congenital factor IX deficiency who developed acquired inhibitors.

Methods Used: Three months post therapy for B-cell Non-Hodgkin's Lymphoma, she acutely developed a hemorrhagic episode while recovering from a respiratory infection. Initial management included fresh frozen plasma without resolution of the bleeding. Recombinant factor VIIa was added until hemostasis was achieved. Investigation of the bleeding episode revealed a prolonged partial thromboplastin time (aPTT) [64.5 sec with normal range 25–35] and a factor IX level of 4% [47–104%] due to the spontaneous development of a weak inhibitor to factor IX (0.07 Bethesda units).

Summary of Results: The patient was then treated with intravenous immunoglobulin (IVIG) at 1 g/kg/day × 2 days and prednisone (2 mg/kg/day once daily for seven days followed by a one week taper). Seven days post immunotherapy there was complete resolution of the acquired factor IX inhibitor with normalization of aPTT and factor IX levels.

Conclusions: No other cases have been reported involving acquired factor IX inhibitors within the pediatric HIV/AIDS subpopulation. It is our experience that the regimen of IVIG and steroids was both successful and safe in the resolution of this rare coagulopathy without further compromising her immunological status. Further studies are warranted to establish a medical standard of care for these patients.

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A MASSIVE INTRATHORACIC MALIGNANT PERIPHERAL NERVE SHEATH TUMOR

A. Udhraim, M. Barnhill *Tulane University School of Medicine, New Orleans, LA.*

Case Report: A 49-year-old African American female with a history of neurofibromatosis type 1 presented to the hospital with dyspnea, dry cough and left upper quadrant abdominal pain for the last 3 weeks. Physical examination revealed tachypnea, tachycardia, normal oxygen saturation on room air, absent breath sounds in the left lung, a left upper quadrant palpable abdominal mass, innumerable café au lait spots and skin freckling.

Chest x-ray illustrated complete opacification of the left hemithorax. Computer tomography (CT) of the chest confirmed a large mass occupying the entire left hemithorax with extension beyond the rib margin with rightward displacement of the heart and esophagus [Figure 1]. CT of the abdomen showed extension of the left hemithorax mass into the left upper abdomen and extending down to the lower pole region of the left kidney.

A CT-guided percutaneous biopsy of the mass illustrated a malignant spindle cell neoplasm consistent with malignant peripheral nerve sheath tumor. The tumor was diffusely positive for S100 as well as vimentin. Tumor was negative for CD 117.

Patient was not deemed a surgical candidate due to the extent of her disease. In an attempt to improve her dyspnea, the patient received palliative radiation to the left chest wall to a total of 2000 cGy given in five fractions. Patient declined systemic chemotherapy. Instead, she elected to receive best supportive care alone and entered home hospice care.



FIGURE 1: CT Scan of chest, coronal view.

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SUCCESSFUL TREATMENT OF CYCLIC THROMBOCYTOPENIA WITH PROGESTERONE THERAPY

AM. Walsh, LM. Hilliard *UAB, Birmingham, AL.*

Purpose of Study: Progesterone therapy resolves bleeding and stabilizes platelet count in patients with cyclic thrombocytopenia.

Methods Used: Case report.

Summary of Results: Cyclic thrombocytopenia (CTP) is a rare disorder of unknown etiology characterized by periodic fluctuations in platelet counts. We describe two patients diagnosed with cyclic thrombocytopenia and treated successfully with progesterone.

Patient 1 Presented with severe menstrual bleeding and thrombocytopenia. Platelet count was 23,000 with hemoglobin of 4.4 g/dl. She responded to platelet transfusion and platelet count continued to increase without further transfusions. She was started on depo-provera and iron. She was lost to follow up and presented a year later with several months of heavy menstrual bleeding. Platelet count was 48,000 with hemoglobin of 5.9 g/dl. She was treated with IV estrogen and packed red blood cells. In three days, platelet count was 96,000 and subsequently increased to 1,424,000. Fluctuations in platelet counts over 6 weeks were: 96k; 1.424 million; 529k; 79k; 503k; 1.156 million; 349k. These fluctuations occurred when patient was on oral contraceptives. Depo progesterone was restarted and platelet fluctuation and bleeding resolved. Patient's mother also describes menorrhagia with thrombocytopenia, was treated for ITP, and had a hysterectomy for recurrent bleeding.

Patient 2 presented with menorrhagia and anemia. Her initial platelet count was 1,182,000 and hemoglobin 7.2 g/dl. Platelet count decreased to 66,000 over two weeks with an increase one week later to 1,364,000. She was started on iron with a steady increase in her hemoglobin without need for a blood transfusion. A bone marrow biopsy showed megakaryocytic hyperplasia without dysplasia. She was started on depo progesterone and since then has had no significant menorrhagia and normalization of her platelet counts. Neither patient nor patient 1's mother ever had bleeding except for menorrhagia.

Conclusions: CTP is a rare disorder of unknown etiology easily confused with ITP. Patients with CTP are often initially treated with ITP therapy if diagnosis is not recognized. Hormonal treatment in our patients ameliorated the platelet cycling and prevented bleeding. Depo progesterone appeared more effective in our patients than oral contraceptives.

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THE ROLE OF PARTIAL LARYNGEAL SURGERY IN TODAY'S ERA OF ORGAN PRESERVATION: RESULTS AND OUTCOMES WITH SUPRACRICOID LARYNGECTOMY - REPORT OF A CASE AND REVIEW OF LITERATURE

RR. Walvekar, V. Zuzukin, DD. Beahm *LSU HSC, New Orleans, LA.*

Purpose of Study: To demonstrate functional outcomes of partial laryngeal surgery and provide a comparison of literature to show oncologic, functional, and quality of life outcomes between partial laryngeal surgery and chemoradiation protocols for laryngeal cancer patients.

Methods Used: Report of a case with review of literature.

Summary of Results: A 44 year old male patient with T2 N0 M0 cancer of the glottis presented to our service with risk factors for developing head and neck cancer. The patient was otherwise healthy with no significant medical co-morbidities and previous relevant surgical history. A panendoscopy was performed to obtain a tissue diagnosis and map the extent of the cancer. Given the limited nature of the cancer, young age, and already hoarse voice, options were presented to the patient of either having an upfront partial laryngeal surgery with adjuvant radiation as necessary versus having definitive chemoradiotherapy. Patient had excellent functional results with partial laryngeal surgery. The patient was swallowing without the need for a tracheotomy tube at post operative day 9. Presence of perineural invasion however necessitated need for adjuvant therapy.

Conclusions: Open partial laryngeal surgery is a feasible option for limited cancers of the larynx in a public hospital setting. Assessment and mapping of the tumor for surgery is critical. Successful outcome require an experienced multidisciplinary team comprising of a head neck oncologic surgeon with expertise in this procedure, radiation oncology, medical oncology, speech and swallowing rehabilitation and supportive nursing care as well as adequate patient education.

Infectious Disease, HIV, and AIDS**Joint Poster Session**

5:00 PM

Thursday, February 25, 2010

170**MULTIPLE SCLEROSIS IN A HIV PATIENT**S. Almaskeen, LS. Engel *LSU Health Sciences Center, New Orleans, LA.*

Case Report: Multiple sclerosis (MS) is an autoimmune disorder characterized by inflammation, demyelination and gliosis. Manifestations of MS vary from benign illness to a rapidly evolving and incapacitating disease.

A 44 year-old woman with HIV, CD4 count 40 / μ L, presented with worsening right sided weakness and diplopia for 5 days. She also complained of slurred speech and tingling of her right leg for the same time but denied nausea, vomiting or fever. She was started anti-retroviral therapy one month prior to presentation but she reported poor adherence.

Her vital signs were normal and her general physical examination was unremarkable. Her neurologic exam revealed sixth nerve palsy in left eye and right upper motor neuron facial palsy. Her speech was slow and slurred. Strength testing was 4/5 in the right upper and lower extremities. Head CT showed low attenuation 1.2 cm focus with surrounding edema in left high parietal region. This was followed by brain MRI which showed focal areas of abnormal T2 signals in pontomedullary, cerebellar, cerebral hemispheric cortices and subcortical white matter areas. Serum toxoplasma IgG was elevated at 11.6 IU/mL (<4.0). CSF examination revealed 24 WBCs/mm³ (100% lymphocytes), glucose 51 mg/dl, protein 43.3 mg/dl. Routine microbiologic studies were negative. CSF cryptococcal Ag, JC virus, EBV, HSV, VDRL were negative. The CSF IgG was elevated at 17.1 IU/mL (0.5–6.1), and the IgG index was 1.6 (0.0–0.7). CSF IgG synthesis rate was at 46.4 (–9.9–3.3 mg/day) and CSF oligoclonal bands was positive. The patient was started initially on broad spectrum antibiotics and toxoplasmosis treatment but after CSF data supported the diagnosis of MS, antibiotics were discontinued and she was placed on high dose IV steroids for 3 days with resultant improvement in her symptoms.

The diagnosis of CNS disorders in HIV patients can be a challenge. Determination of degree of immunosuppression can help guide the differential diagnosis. While benign and malignant brain tumors and metastases predominate in immunocompetent hosts, opportunistic infections and AIDS-associated tumors, such as primary CNS lymphoma should be considered in severely immunosuppressed patients. Alternative diagnoses should also be considered if the patient is not responding to treatment.

171**PROPIONIBACTERIUM IN SAPHO : RED HERRING OR ETIOLOGY?**B. Bagga^{1,3}, LM. McGregor², JL. Shenep^{1,3} ¹*St Jude Children's Research Hospital, Memphis, TN;* ²*St Jude Children's Research Hospital, Memphis, TN and* ³*University of Tennessee Health Sciences Center, Memphis, TN.*

Case Report: A 14 year old boy presented with insidious onset of painful swelling of the left clavicle. Radiograph showed a poorly defined lytic lesion suspicious for malignancy in the medial and mid clavicle. His only other symptom was intermittent knee pain. Exam revealed a well appearing adolescent with moderate acne and diffuse, mildly tender swelling without erythema or warmth over the left clavicle. Further imaging revealed a sclerotic tibial lesion and bone scan showed increased uptake in the clavicular and tibial sites. CBC was unremarkable and blood culture was negative. ESR and CRP were mildly elevated. Serology for infectious causes of osteomyelitis was negative. Biopsy of the clavicular lesion suggested osteomyelitis; culture grew *Propionibacterium acnes* in broth only. Given the biopsy results, clindamycin was initiated. Due to lack of clinical and radiological improvement after 8 weeks, clindamycin was discontinued and NSAID therapy initiated. After 12 weeks of NSAID therapy, clinical and radiological improvement was evident. Our patient's course is consistent with SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis, Osteomyelitis). Chronic recurrent multifocal osteomyelitis (CRMO) and sternocostoclavicular hyperostosis are the main features of SAPHO. The etiology of this disease is unclear; however, a few cases have been associated with *Propionibacterium*. In our patient, *P. acnes* may have contaminated the biopsy specimen due to acne of the skin overlying the biopsied lesion. This hypothesis is supported by lack of improvement with clindamycin and

subsequent improvement with NSAID. SAPHO has attracted considerable attention in the orthopedic and rheumatology literature during the past decade, but there is a dearth of literature in general pediatrics, infectious diseases and oncology. Diagnosis of SAPHO can be especially challenging in pediatrics due to inconsistent dermatologic findings. This report serves to increase awareness of this entity, leading to early diagnosis, judicious use of antimicrobials and possible insight into the role of *Propionibacterium* in the pathogenesis of this intriguing syndrome.

172**SAVING HER NEMESIS FROM HEMATEMESIS**SK. Chilakala, R. Philip, G. Balasubrahmanyam, D. Macariola, T. Aiken *ETSU, Johnson City, TN.*

Case Report: 16 y/o previously healthy female presented to the ER with a 1 day h/o hematemesis. Suspecting NSAID induced gastritis was admitted for observation. She gradually deteriorated overnight and had severe hematemesis and black stools. No h/o trauma or recent infections. PMH: Unremarkable except for a remote history of low platelet count reported as benign by hematology. PE: Well appearing female, T 98.5, P 82, RR 21, clear lungs, normal heart sounds, no abdominal tenderness, splenomegaly without hepatomegaly and a normal neurological exam. WBC 12,000, Hb/Hct 8.3/24.6. EGD done for continued hematemesis showed multiple varices at the distal esophagus, which were banded at that time. Bleeding and clotting disorders were ruled out with extensive lab work all being normal. CT abdomen showed hepatic heterogeneity with intrahepatic biliary ductal dilatation and portal hepatic adenopathy and calcifications resulting in portal hypertension. Despite paucity of lung symptoms, the calcifications led us to do CT Chest which showed diffuse calcifications on the lungs. Liver biopsy revealed focal microgranulomata. Eventual infectious disease workup was positive for *Histoplasma capsulatum* (1:32) and negative for diseases such as HIV and Hepatitis. Patient was initially started on Amphotericin B until urine histoplasma antigen was noted to be 4ng/ml. Consequently, the patient was started on Itraconazole and monitored closely. The patient is currently doing well.

Hematemesis in the pediatric age group is in itself unusual and requires further workup. Certainly, Histoplasmosis as a cause requires a high index of suspicion. Histoplasmosis infection develops when histoplasma conidia are inhaled into the lungs and the organism is disseminated throughout the RES. Infection is self-limiting in immunocompetent individuals. It is very unusual for a healthy immunocompetent patient with no known risk factors to present with disseminated histoplasmosis. In this child there is no h/o documented previous histoplasmosis, no h/o re-infection and no risk factors. We therefore present this case to highlight the unusual presentation in pediatric patients. More importantly, for the clinician to highlight the significance of hematemesis in this age group and to reiterate medication induced gastritis as a diagnosis of exclusion rather than the rule.

173**SERONEGATIVE NEUROSYPHILIS IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS: TRANSFORMATION FROM THE GREAT IMITATOR TO THE GREAT MASQUERADER**R. Corona¹, P. Larppanichpoonphol^{1,2}, R. Kimbrough^{1,2} ¹*Texas Tech University Health Science Center, Lubbock, TX and* ²*Texas Tech University Health Sciences Center, Lubbock, TX.*

Case Report: From the CDC report, the incidence of syphilis has been on the rise, especially in homosexual men with HIV infection, after reaching an all-time low in 2000. The diagnosis and treatment of this highly infectious disease has always presented a dilemma given its diverse presentations and varied clinical course, hence the name "the Great Imitator". Recent reviews and studies have documented altered clinical presentations and serologic response, further complicating its diagnosis and treatment. More specifically is the presentation of ocular syphilis, which is often misdiagnosed as another AIDS-defining illness, most notably CMV retinitis. Ocular syphilis has been reported in several seronegative cases. These reports describe a prozone phenomenon as the basis for negative RPR screening test, which after appropriate dilution renders the positive RPR. We present a case of ocular syphilis in a patient with AIDS, who had 2 previously negative RPR tests.

A 53-year-old white man with AIDS presented with sudden blindness. He had negative RPR and CD4+ cell count of 63/L, 2 months prior to the

symptom. Ophthalmologic examination revealed panuveitis, chorioretinitis, and retinal detachment, which led to a diagnosis of CMV retinitis. However, after no improvement with treatment and continued worsening, an FTA-ABS was ordered and was positive. A repeat RPR became positive after serial dilutions. He also had a reactive CSF VDRL test. Treatment for neurosyphilis was initiated.

We present a case of ocular syphilis as a manifestation of neurosyphilis in a patient with AIDS, despite HAART. We report and review the resurgence of neurosyphilis and the alterations to its clinical presentations and serologic response in HIV-positive patients. CD4+ cell count < 350/L has been identified as a risk factor for neurosyphilis in HIV-positive patients. Symptomatic early neurosyphilis has been observed in 30–60% of patients; 50% of early neurosyphilis present with ocular diseases. As syphilis still co-infecting in HIV-positive patients, it's imperative that clinicians exclude ocular syphilis as a cause of visual symptoms in AIDS patients.

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THE AORTIC VALVE INHABITANT

J. Duet, LS. Engel, B. Lo *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: Candida species are the most common cause of fungal endocarditis (24% *C. albicans*, 28% other Candida species). Risk factors for Candida endocarditis include intravenous drug use, indwelling central venous catheters, prolonged fungemia, and prosthetic heart valves. Patients with endocarditis secondary to fungemia typically present with similar symptoms as bacterial endocarditis; however, they tend to have a delayed diagnosis with high rates of relapse. A 51 year old man with history of hypertension, hepatitis C, schizophrenia, seizure disorder, and end-stage renal disease on hemodialysis (via a permacath) presented with a low grade fever and nonspecific complaints of malaise and nausea which are common for him after a dialysis session. Physical exam revealed no overt signs of infection, but did reveal an early diastolic murmur at the right sternal border. It was unknown if this murmur was present previously. Blood cultures drawn in the emergency department grew Candida parapsilosis in both bottles. He was started on micafungin, but continued to have low grade temperatures with occasional spikes. A transthoracic echocardiogram showed an aortic valve vegetation. Tran esophageal echocardiogram revealed that the vegetation was 7mm x 6 mm and attached to the non-coronary cusp of the aortic valve. Repeat blood cultures were consistently positive. An antifungal sensitivity panel for *C. parapsilosis* was consistent with a pan-sensitive organism. After consultation with infectious disease and cardiothoracic surgery, the patient was scheduled for valve replacement surgery in order to treat the fungal endocarditis with a plan to continue lifelong antifungal therapy with fluconazole.

Studies comparing antifungal therapy alone with surgical intervention are somewhat conflicting. However, it is clear that the mortality rate with Candida endocarditis is high, ranging from 30 to 59 percent. Despite the conflicting therapies, the current Infectious Diseases Society of America guidelines recommend a combined approach of antifungal agents and valve replacement for treatment of both native and prosthetic valve Candida endocarditis.

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SYPHILITIC PROCTITIS IN A YOUNG MAN

RA. Goldberg, J. Arteh, E. Nyenwe *University of Tennessee Memphis, Memphis, TN.*

Case Report: Proctitis due to *Neisseria gonorrhoeae* and *Chlamydia trachomatis*, are not uncommon in men who have sex with other men, but syphilitic proctitis is not as common. We hereby report a case of syphilitic proctitis in a young man.

A 39-year-old man was admitted with a month's history of tenesmus, proctalgia, constipation and lower abdominal discomfort. He developed fever and chills 4 days before presentation, but had no hematochezia, respiratory or genitourinary symptoms. His medical history was significant for HIV treated with antiretroviral agents (CD4 count- 440/uL). He was a homosexual man who engaged in unprotected anoreceptive intercourse; and had met a new partner two months before his illness.

Physical examination revealed a well nourished young man who was not ill-looking. His vital signs were stable except for pyrexia of 101 F. Cardiopulmonary examination was unremarkable. He had mild diffuse lower abdominal tenderness without guarding, rebound tenderness or organomegaly. Bowel sounds were normal. Rectal examination elicited anal tenderness

but no masses or external anal lesions. His stool was brown in color with negative occult blood. He had no peripheral lymphadenopathy or skin rash.

Computed tomography of the abdomen revealed multiple pelvic and perirectal lymphadenopathy with stranding of adjacent fat. Further ancillary investigations showed reactive RPR with positive MHA-ATP. Blood, urine and stool cultures did not grow any pathogens. Stool microscopy was negative for ova and parasites. Gram stain and culture of urethral, pharyngeal and rectal specimens were negative for *Neisseria gonorrhoeae*. He underwent sigmoidoscopy which revealed mucosal erythema with submucosal punctate hemorrhage of the distal 7–8 cm of the rectum with no ulcerations. Histology of rectal biopsy showed acute proctitis with multiple granulomas but no neoplastic changes. Acid fast, silver and immunostains were negative for mycobacteria, fungi and CMV.

He was treated with benzathine penicillin and Doxycycline to which he responded remarkably. This case demonstrates that a high index of suspicion is sometimes needed to diagnose syphilitic proctitis. A good clinical history, physical examination and prudent use of ancillary investigations remain invaluable tools in the diagnosis of this easily treatable disease.

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NOVEL INFLUENZA A (H1N1) VIRAL INFECTION IN LATE PREGNANCY: REPORT OF A CASE

BJ. Hymel *LSUHSC New Orleans, New Orleans, LA.*

Case Report: Abstract: Health care workers, including anesthesia providers, are often exposed to different infectious disease processes. In the operating room, anesthesia providers, nursing, and surgical staff utilize universal precautions as a standard of practice. The novel influenza A (H1N1) epidemic has heightened concerns in as much as diagnosis is often delayed and transmission can affect those in a close radius to the infected host. The objectives of this report will be to describe the intensive care management and outcomes of severe H1N1 viral infection in a pregnant patient in the last trimester and to review the epidemiology, management, and outcomes of similar US cases.

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LINGUAL LEISHMANIASIS COMPLICATING VISCERAL DISEASE

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Case Report: 50-year-old National Guardsman, deployed to Saudi Arabia during Operation Desert Storm in 1991 and to Iraq and Kuwait during Operation Iraqi Freedom (2002–2003), presented with a 2 week history of a tongue lesion. A 1.5 cm central cavity lesion and a smaller 0.5 cm lesion lateral to the midline were noted on exam. The platelet count was 115,000/mm³. AST and ALT were 113 U/L and 132 U/L respectively and the alkaline phosphatase level was 571 U/L. Incisional biopsy revealed squamous papilloma. During the subsequent 15 weeks, 4 additional lesions developed. Laser excision biopsy showed marked non-caseating granulomas. The lesions continued to worsen and 2 weeks later, a partial glossectomy was done.

Histopathologic examination revealed numerous intra-cellular amastigotes. Serum antibody against human immunodeficiency virus (HIV) and hepatitis A, B and C were negative. Bone marrow biopsy revealed granulomas. Additional confirmatory testing performed by the Leishmania Diagnostic Laboratory at Walter Reed Army Institute of Research included a positive Leishmania genus-specific PCR of the tongue sample and a rK39 dipstick assay was strongly positive. Treatment consisted of liposomal amphotericin B 3 mg/kg intravenously on days 1–5, followed by additional doses on days 9, and 16. Leishmaniasis of the tongue is not commonly reported. It has been described among immunocompromised patients with HIV, malignancy, organ transplant, and corticosteroid use. Various laboratory abnormalities can be seen with visceral disease including thrombocytopenia and elevated liver function tests.

Definitive diagnosis of leishmaniasis requires demonstration of the organism by histology, culture, or PCR. In our case, definitive diagnosis of mucocutaneous involvement was made by the visualization of amastigotes and positive PCR from the tongue biopsy. Visceral involvement was suggested by the presence of granulomas in both the liver and the bone marrow. The rK39 dipstick assay, which was strongly positive in our patient, detects antibodies against a recombinant antigen found in *L. infantum-chagasi*. The

test is highly suggestive of visceral leishmaniasis with an overall sensitivity of 93.9% and specificity of 90.6%.

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2009 H1N1 INFLUENZA (2009 H1N1) PNEUMONITIS IN DOUBLE LUNG TRANSPLANT PATIENT

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Purpose of Study: Report and review 2009 H1N1 pneumonia in a transplant recipient.

Methods Used: Case Report.

Summary of Results: Since the CDC first reported 2 cases of 2009 H1N1 infection in April, 9,079 admissions and 593 deaths associated with this infection were reported up to 08/30. A recent CDC study of 2009 H1N1 in the US reported pneumonia in 100/249 cases between April and June. 73% of the patients had chronic medical conditions; 15% were immunocompromised. Two reports of 2009 H1N1 pneumonia outside the US noted chronic medical diseases in 50% of cases, but none had organ transplant. We present a case of 2009 H1N1 pneumonia in a 26 year-old woman, who underwent a double lung transplant 1 year ago. She presented in July with pleuritic chest pain and productive cough for 2 days. There had been no wide spread of seasonal influenza or 2009 H1N1 in the community before her presentation. Her vital signs were temperature of 99.6°F, respirations of 20/min, and oxygen saturation of 98% on O₂ 2L/min. Initial tests were notable for WBC count of 6,900/L (82% neutrophils), ALT 100 U/L, AST 55 U/L, alk phos 605 U/L, LDH 317 U/L, and CPK 54 U/L. Her chest CT showed infiltrates in both lower lung zones. Piperacillin-tazobactam was started. A bronchoscopy was performed to exclude opportunistic infections. She progressed into respiratory distress and required intubation on day 6. On day 13, 2009 H1N1 was amplified from BAL by PCR and oseltamivir was started. She was later transferred to the original transplant hospital.

Conclusions: We report a case of 2009 H1N1 pneumonia in a transplant patient. Investigation to exclude opportunistic infections in transplant recipients is a standard practice. However, both seasonal and emerging infections can well occur in this population. From a 10-year study of influenza in solid organ transplants, more cases have been noted in lung transplant. Transplant patients are reportedly at risk of serious complications from influenza. 2009 H1N1 has been increasingly reported in immunocompromised hosts, including transplant recipients. Clinicians need to be aware of influenza and 2009 H1N1 in this population, and provide empirical treatment as appropriate.

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AN UNUSUAL PRESENTATION OF PCP: TO TREAT OR NOT TO TREAT?

L. Nguyen, LS. Engel *LSU-Health Sciences Center, New Orleans, LA.*

Case Report: *Pneumocystis jirovecii* (PJP; formerly *Pneumocystis carinii*) is a common opportunistic infection in HIV patients, particular in those with a CD4 count less than 200. A 29-year-old man with a history of HIV/AIDS (CD4 of 118 cells/mm³) and poor medical compliance with his highly active anti-retroviral therapy presented to the emergency department with shortness of breath, productive cough, and subjective fever and chills for 3 days. The patient reported some mild dyspnea on exertion as well as two episodes of post-tussive emesis but denied abdominal pain, diarrhea, and sick contacts. At presentation, the patient was found to be febrile with a temperature of 104.6°F. His pulse and blood pressure were unremarkable and he had an oxygen saturation of 100% on room air. On physical exam, he had slightly decreased breath sounds throughout without dullness to percussion, changes in tactile fremitus, or crackles. Serum chemistries included a white blood cell count of 10.6 × 10³ cells/mm³, an LDH value of 203 U/ml, and unremarkable arterial blood gases. Chest x-ray demonstrated 2cm × 2 cm opacity with central lucency in the right mid-lung zone. The patient was treated with antibiotics empirically for pneumonia and received prophylactic dosing of sulfamethoxazole/trimethoprim for *Pneumocystis* prevention. Sputum smears for PJP were found to be positive, and the patient's therapy was converted to full treatment dosing of sulfamethoxazole/trimethoprim for *Pneumocystis* infection. The patient's symptoms improved significantly with treatment. *Pneumocystis jirovecii* is the most common opportunistic infection in HIV-infected patients and should be suspected in patients with fever,

cough, progressive dyspnea with decreased oxygen saturation on exertion, an elevated LDH, and an increased A-a gradient. Classic radiographic evidence for PJP infection includes diffuse bilateral infiltrates. Atypical x-ray findings such as segmental infiltrates, cysts, nodules, or effusions may also be present. However, chest x-rays may be initially normal in up to one-fourth of patients. Definitive diagnosis requires documentation of the organism in a respiratory specimen.

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"TREATED THE HORSE BUT FORGOT THE ZEBRA": A CASE OF NEUROCYSTICERCOSIS

SR. Ruziev, CL. Moll, LS. Engel *LSU Health Sciences Center, New Orleans, LA.*

Case Report: A 27 year-old Latin American woman presented to the emergency department after 5 minutes of tonic-clonic seizure activity. She also complained of headaches, vision changes, and nausea and vomiting of one week duration. Her past medical history was significant for HIV/AIDS (CD4 count of 64 cells/mm³), cytomegalovirus (CMV) retinitis and toxoplasmosis diagnosed 2 weeks earlier. She was on antiretroviral therapy as well as therapy for toxoplasmosis and CMV. She had emigrated from Honduras two years ago and was unable to recall how she contracted HIV. She did not smoke, drink alcohol or use illicit drugs. Her father passed away from a brain aneurysm at 69 years of age. At the time of admit, her vital signs were unremarkable and physical exam revealed a quadranopsia of her right eye. The remainder of the physical examination was unremarkable. Urinalysis was suggestive of a urinary tract infection and labs were consistent with acute renal failure. An initial cat scan of her head showed the lesions of toxoplasmosis, unchanged from a previous scans two weeks prior. Furthermore, there was a lesion suggestive of a scolex in the frontoparietal region. MRI of the brain confirmed the findings of neurocysticercosis (NCC). Treatment with albendazole was initiated. She was also continued on her anti-retroviral and toxoplasmosis therapies. Ophthalmology was consulted to evaluate the right quadranopsia and agreed with the previous diagnosis of CMV retinitis. She was started on intra-vitreous ganciclovir. The patient had no further seizures and the remainder of her hospital stay was unremarkable..

NCC is the most common parasitic disease of the nervous system and the major cause of acquired epilepsy in developing countries. Patients typically present with seizure activity as well as headache from intracranial hypertension. Diagnosis is based primarily on neuroimaging findings. Given the rarity of native NCC disease in the United States, misdiagnosis is common. However, with increased immigration and travel to and from endemic areas such as Latin America, the prevalence of NCC is increasing and should be considered in patients with unexplained seizure activity.

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COCCIDIOMYCOSIS CAVITARY LESION OF THE LUNG, TREAT OR NOT TO TREAT?

S. Sanne¹, B. Corcoran¹, M. Borissov¹, R. Mathew², LS. Engel¹ ¹LSU Health Sciences Center, New Orleans, LA and ²LSU-Health Sciences Center, New Orleans, LA.

Case Report: The responsible agent of Coccidiomycosis (Valley Fever) is *Coccidioides immitis*. This fungus is found in the soil and is endemic in the Southwestern United States. Symptoms of infection occur approximately 1–3 weeks after exposure and include fever, cough, chest pain, headache and myalgias. Immunocompetent patients usually have a sub-clinical picture requiring no intervention.

A 26-year old woman with a history of Valley Fever presented to the emergency department with a 6 days of pleuritic chest pains associated with coughing. The patient reported similar pleuritic chest pain that occurred 1–2 times per year since being diagnosed with Valley Fever in 2002. The patient noted that her roommates had recently experienced upper respiratory symptoms, including myalgias, headache and cough. Upon admission, the patient was stable and indicated her symptoms had been improving. Her physical exam and laboratory data were unremarkable. A chest x-ray revealed a hyper-lucent area in the left suprahilar region. Subsequently a chest CT scan revealed an irregular thin walled cavitary lesion. Sputum cultures only grew normal flora and cultures for acid-fast bacilli were negative. Blood cultures did not grow and the result of her HIV test was also negative. Serum *Coccidioides* antigen testing revealed a 1:8 titer. The patient was diagnosed

with cavitary lesion secondary to coccidiomycosis and subsequently discharged from the hospital without antifungal treatment.

Cavitary lesions occur in approximately 4-8% of coccidioid infections and usually resolve within first two years of infection. The inflammatory response to the fungal infection results in areas of infarction, creating cavitations. A residual cavity can occur that is usually solitary, thin walled without discernible infiltrate and located in the periphery of the lung. In the absence of symptoms (pleural discomfort, hemoptysis, cough) treatment is not warranted. Periodic imaging can be done in order to monitor cavities. If symptoms are present then antifungal agents (fluconazole) can be implemented but symptoms may recur if treatment is discontinued. Surgical intervention is only required if symptoms persist despite antifungal treatment.

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CMV ENCEPHALITIS IN THE HAART ERA

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Case Report: Purpose of Study: To perform a literature review of CMV encephalitis.

Methods Used: Descriptive Case Report Study.

Summary of Results: Cytomegalovirus (CMV) disease is one of the AIDS-defining illnesses and has several clinical presentations, including encephalitis. In the pre-highly active antiretroviral therapy (HAART) era, an autopsy study of AIDS cases showed CMV as the second neuropathological finding, accounting for 22% of 390 cases. The incidence of CMV disease has declined from 7.34 cases in the pre-HAART to 0.75 cases in the HAART era per 100 patient years. But cases of CMV encephalitis have continued to be documented in patients with no medical care. We report a recent case of CMV encephalitis in an ART-naïve patient with CD4+ cell count of 0/L. A 41 year-old Hispanic man, who never sought treatment for HIV infection for 20 years, presented with acute mental status changes. His vital signs were normal except for tachycardia. He was disoriented, uncooperative, and hardly followed commands. There was no nuchal rigidity or focal neurological deficit. The rest of physical examination was unremarkable. His HIV-1 RNA level was 778,000 copies/mL. A gadolinium-enhanced MRI scan of the brain showed ependymal enhancement of the lateral ventricles and ill-defined hyperintense foci in the cerebellum, indicative of ventriculitis. A laboratory examination of the CSF showed RBC of 13/ μ L, WBC of 4/ μ L (83% lymphocytes), total protein level of 248 mg/dL, and glucose level of 29 mg/dL. CSF cryptococcal antigen and VDRL were negative. CSF CMV DNA > 2,000,000 copies/mL was amplified by PCR. He had no CMV retinitis. A 21-day course of ganciclovir was given, and daily valganciclovir was started for maintenance therapy. His mental status improved. A 3-month follow-up MRI scan showed improvement of encephalitis with minimal enhancement of the lateral ventricles. He was able to manage activities of daily living. ART was to be started on his next follow-up.

Conclusions: We report CMV encephalitis, now an uncommon but still fatal opportunistic infection. Confirmed encephalitis is based on the detection of CSF CMV DNA, CMV culture in CSF, or brain biopsy. Optimal treatment for CMV encephalitis is not established, but combination of ganciclovir and foscarnet might be preferred. A delay to start ART in patients with CMV encephalitis is recommended.

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RESPIRATORY INFECTIONS-HOW MANY IS TOO MANY?

E. Song, R. Philip, S. Chilakala, D. Macariola, G. Balasubrahmanyam
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Case Report: 7 1/2 y/o Caucasian male presents with a h/o productive cough and fever for 6-8wks, tmax 103F. Diagnosed with pneumonia at PCP's office and initially treated with amoxicillin. Despite this, he developed worsening right sided chest pain. He continued with fever, chest pain, abdominal pain, SOB and vomiting. CBC revealed leucocytosis warranting admission. PMH: nl till 1yr then recurrent sinusitis and ear infections. Meds: Albuterol PRN. Immunizations UTD. FMH: Questionable CF, paternal grandfather needed monthly IVIG infusion. P/E: T 101.5F, HR 170, RR 42, BP 98/67, wt 21kg (<5th%) HEENT: tympanostomy tubes. Lungs: dull to percussion Rt LL, crackles Rt UL & LL. After blood cultures drawn, he was treated with vancomycin, ceftriaxone. Labs: IgG <200, IgA <6, IgM 40 CH 50: 74, Cold agglutinins, sweat chloride, NOBT and PPD skin test were all negative. Ab

levels for tetanus and H.influenza type b non protective. CXR: opacification of lower Rt base, effusion of right lung apex. Bronchoscopy: edema of right bronchus without purulent secretions. He underwent thoracentesis, scant serosanguinous fluid obtained. Bronchial washing and pleural fluid - S.pneumoniae isolated susceptible to ceftriaxone, intermediate resistance to amoxicillin. No AFB or fungus isolated. Worsening tachypnea warranted decortication. He completed 12 days of IV ceftriaxone followed by 10 days of oral amoxicillin. He is receiving monthly IVIG infusion.

Discussion: This case brings to light the debate on how many infections differentiates a "normal but unlucky child" from one with primary immunodeficiencies. It also exemplifies the importance of a thorough history and good documentation of the sick visits in ambulatory care. The red flags that a general pediatrician needs to look out for include delayed growth, slow therapeutic response to antibiotics, suppression rather than eradication of bacterial infection and unexpected complications of a fairly simple infection. Furthermore, a child who was doing well up to one year and then developing recurrent infections should alert pediatricians to look for immunodeficiency as possible reason. All of these pointers are well exemplified in this case. As most immunodeficiencies are familial, a good specific family history must be taken. Management entails IVIG and a low threshold for antibiotic usage.

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THE OTHER GRAM-POSITIVE ROD: A CASE OF BACILLUS CEREUS SEPSIS IN A PREMATURE NEONATE

BM. Statham¹, D. Kurepa², M. Gardner³, SM. Hussein² ¹LSUHSC Shreveport, Stonewall, LA; ²LSUHSC-Shreveport, Shreveport, LA and ³LSUHSC-Shreveport, Shreveport, LA.

Case Report: Bacillus cereus is a gram-positive bacterium found in dust, air and water. The organism is most known for its role in self-limiting food borne illness, but has gained increasing awareness the past few decades as an invasive pathogen affecting the critically ill with intravenous catheters and shunts. We report a case of B.cereus bacteremia and subsequent sepsis in a 7 day-old, 1531 gram, twin male neonate born at 29 week gestation with multiple congenital anomalies, including imperforate anus. Maternal history was suspicious for chorioamnionitis, otherwise unremarkable. The neonate had an umbilical artery catheter (UAC) placed shortly after birth and was began on empiric antibiotics. On day 3 the infant was taken to the operating room for a gastrostomy tube, diverting colostomy for imperforate anus and LADD procedure for malrotation, followed by a JP drain and t-tube placement for duodenal perforation. A PICC line was placed for central venous access. The patient developed persistent bacteremia and blood cultures were drawn on day 7 of life from the UAC and PICC line, in which returned positive for large gram-positive rods, and later reported as 'Bacillus species other than B.anthraxis'. The pathogen was identified at an outside laboratory as Bacillus cereus. The neonate continued to have bacteremia despite antibiotic treatment and discontinuation of the UAC and PICC. There are only a small number of documented cases of clinically significant B.cereus bacteremia in the neonatal population. This case highlights the difficulty in diagnosing and treating this invasive pathogen in the premature neonate, especially with persistent requirements for invasive lines and tubes, such as the t-tube and gastrostomy tube in our patient. The clinician should have a heightened awareness of B.cereus as 'the other gram-positive rod', (next to Listeria) that can affect the neonatal population.

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A CASE OF STAPHYLOCOCCUS SCALDED SKIN SYNDROME AND SEPTICEMIA IN ADULTS

H. Zainah, F. Cheema
Henry Ford Hospital, Detroit, MI.

Case Report: Staphylococcus Aureus causes staphylococcus scalded skin syndrome (SSSS). It is usually reported in newborns but is a rare disease in adults with high mortality rates. We describe a case of SSSS in a patient with an underlying kidney disease (CKD).

A 56year old female patient with CKD presented with diffuse rash involving the upper and lower extremities for one day duration. Two weeks prior to presentation, she had a left forearm arteriovenous graft loop created. On post operative day twelve, she noticed pruritic erythematous rash around the graft surgical site, which was thought to be due to frequent dressing changes. Two days later, the rash spread within few hours across the head, neck, torso, abdomen, and extremities sparing palms, soles and mucous membranes. No blister formation or specific dermatomal distribution was

noted. The patient experienced subjective low grade fever, chills and diaphoresis. Exam revealed wide spread confluent erythematous macules with de-epithelialization on areas of friction in addition to pustules and flaccid bullae. Nikolsky sign was positive.

Blood tests were remarkable for leukocytosis of 16000 and worsening of renal failure. The patient Developed septic shock and was intubated. Skin biopsy revealed intracorneal and subcorneal cleft with papillary edema and inflammatory infiltrate in the superficial dermis pathognomonic for Staphylococcus scalded skin syndrome. SSSS diagnosis was favored. Patient was started on anti-staph toxin antibiotics with clinical improvement.

SSSS diagnosis is usually made by characteristic clinical presentation, histological findings (intraepidermal cleavage at level of superficial/granular layer) and isolation of exfoliative toxin-producing Staphylococcus Aureus. SSSS in adults has higher incidence of SSS septicemia especially with underlying risk factors such as CKD as in our patient, therefore it is essential we recognize SSSS early in the course of the disease, because of associated increased mortality.

Medical Education and Medical Ethics

Joint Poster Session

5:00 PM

Thursday, February 25, 2010

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ANSWERS TO QUESTIONS ABOUT ETHICS TO MEDICAL STUDENTS IN POETRY AND PROSE

BF. Andrews *University of Louisville, Louisville, KY.*

Purpose of Study: Medical students especially from the University of Louisville School of Medicine as well as pediatric residents, fellows and faculty have gifted me with profound questions about medicine and other areas for nearly half a century. Those about ethics and duty stand out for frequency and interest.

Methods Used: A selection of these requested statements and poems have been collected over the years. The first statement "The Responsibility of the Physician" has been received by all University of Louisville Medical School graduates since 1965. In 1972, it was altered by Ross Laboratories when they changed the word physician to pediatrician and then with permission sent the statement everywhere their products were distributed without use of Ross Laboratories on the statement. Also, in 1972 medical students from University of Louisville asked for a definition of ethics for doctors and gave two weeks for a response. "Ethics is the highest possible level of moral thought and action...", (closing with Marcus Aurelius, "If it is not true, do not say it. If it is not right, do not do it") was the answer.

Summary of Results: "Duty," "To Strive Against Iatrogenesis...", "A Statement on Transplantation and Organ Donors," "The Children's Bill of Rights," and "Medicine is More Than a Profession" are other statements that were made in answer to questions regarding many ethical dilemmas.

Conclusions: The use of poetry which is easily remembered is a most effective tool for teaching ethics.

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IT'S NOT JUST ENGLISH AND SPANISH: LESSONS LEARNED FROM USING HEALTH LITERACY STRATEGIES IN A COMMUNICATION SKILLS PROGRAM

R. Connelly¹, T. Turner², A. Giardino^{2,3}, X. Tran³ ¹University of South Alabama, Mobile, AL; ²Baylor College of Medicine, Houston, TX and ³Texas Children's Hospital, Houston, TX.

Purpose of Study: 1) To describe the effects of a pilot program on providers' knowledge and use of health literacy strategies; 2) To understand reasons for participating in communication skills program; and 3) To describe participants' opinions regarding the program's delivery and content.

Methods Used: This was a quasi-experimental study design using a questionnaire before and immediately after the program, and one and three months afterwards. Semi-structured interviews one year after the intervention explored participants' opinions about the program.

Summary of Results: Of 180 and 177 providers invited, only 10 and 3 participated in two program offerings. Immediately after the program mean knowledge score was significantly higher (59.2 vs. 80, $p < 0.001$). Reported awareness of health literacy issues increased from 23.1% to 92.3% ($p < 0.001$).

Mean knowledge score was not different at 1 month (71.5, $p > 0.005$), but was significantly lower at three months (63.3, $p < 0.005$). Increased awareness of health literacy issues remained high at one and three months after the program. Using simple language, limiting amount of information and checking for understanding were strategies reportedly used at one and three months follow up. Based on semi-structured interviews with participant volunteers, some reasons for participating in the program were willingness to improve communication skills and realization of the gaps in communication with patients. The information presented was 'eye opener'; communication was 'more than translation or speaking same language'. Health literacy strategies were described as simple to use after getting used to them.

Conclusions: Our program increased participants' knowledge and awareness of health literacy issues and reported use of health literacy strategies for communication for up to three months. Health literacy strategies were well received and reportedly simple to use. Outcome measures in the future should seek to include objective measurement of health literacy strategies utilized by providers, effects of strategies use on provider-patient communication, as well as patients' opinions about these strategies.

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STUDENTS' ENGAGEMENT IN LONGITUDINAL CLINICAL EXPERIENCES

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Purpose of Study: The purpose of the present study is to report students' choices regarding longitudinal clinical experience (LCE) placements. Qualitative data will also be provided regarding the subjective experiences of first-year medical students in these placements.

Methods Used: The study employed a mixed methods approach. As a component of a behavioral science course, all first-year medical students are required to complete a LCE. This involved shadowing a local clinician in his or her practice for six visits. LCE sites included primary care and myriad specialized care settings. Students were required to submit a reflective essay on their experience following each visit. These data are but one component of a student portfolio required of all first-year medical students. Researchers descriptively analyzed the types of setting selected by the students. A rubric was developed to evaluate and select written portfolio pieces for inclusion in this study. These data will provide a greater understanding of the students' subjective experience of LCEs.

Summary of Results: Essays were gathered over a two-year period contributing to a total sample size of 150 first-year medical students. Analysis of these data is pending.

Conclusions: These data will provide medical educators with insight into the subjective experiences of first-year medical students engaging in early clinical experiences. In addition, educators will have greater understanding of student's participation in portfolio-based assessment. Using portfolio-based assessment facilitates a relationship between educator and student that is reciprocal and meaningful.

Pediatric Clinical Case

Joint Poster Session

5:00 PM

Thursday, February 25, 2010

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THE EVALUATION OF A FEVER IN A PEDIATRIC TRAVELER

P. Acharya, J. Zayas *University of Florida, Jacksonville, FL.*

Case Report: Typhoid fever is a disease that can commonly occur among travelers to Southeast Asia and Africa. Our patient was a seven year old Southeast Asian female who was completely asymptomatic besides having a fever and chills. A blood culture was drawn only because she had traveled to India one month ago. Her blood culture was positive for Salmonella Typhi. She was unable to return to school until she had three negative stool cultures for Salmonella Typhi. The lesson learned from this case is that it is important to ask at regular checkups if there are any plans for travel to other countries, especially if the patient originates from that country. If future travel plans are known to the pediatrician at least one month in advance, the patient can receive the appropriate vaccines to prevent such illnesses to ensure a happy and safe travel and a healthy transition back into the United States.

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BLUE RUBBER BLEB NEVUS SYNDROME: A RARE SYNDROME WITH POTENTIALLY FATAL COMPLICATIONS DIAGNOSED INCIDENTALLY

R. Arbizu, L. Crews *University of South Alabama, Mobile, AL.*

Case Report: A ten year old female presented to the clinic with history of an upper respiratory infection. Incidentally upon examination, multiple nodular skin lesions were observed on the left lower abdomen and right upper extremity. After further questioning, the patient stated that the abdominal lesions appeared initially several years prior after a minor trauma to the region producing an initial abrasion. After a short period of time, the lesion became thickened and raised presumed to be a keloid. The arm lesions had appeared much later without a history of trauma and persistently remained with bluish discoloration. These lesions were flat to the surface and easily compressible. The patient was referred to the geneticist where the diagnosis of BRBNS was made. Further evaluation by the gastroenterologist and an ophthalmologist were scheduled.

Discussion: Blue Rubber Bleb Nevus Syndrome (BRBNS) is a rare autosomal dominant condition characterized by multiple cutaneous venous malformations in association with visceral lesions. The most potentially fatal malformations usually involve the gastrointestinal tract; however, almost all organ systems may be involved including the central nervous system, thyroid, parotid, eyes, oral cavity, musculoskeletal, oral cavity, lungs, kidney, liver, spleen, and bladder. The morbidity and mortality associated with BRBNS depends on the extent of visceral organ involvement. The majority of the patients have a normal life expectancy with the cosmetic complications. However, some patients may have severe hemorrhage from the gastrointestinal tract which may require serial transfusions and can be potentially fatal. Bony lesions and joints lesions although not usually fatal may result in significant discomfort, deformity, and debilitation.

Methods Used: Case study.

Summary of Results: We present the case of a 37 week gestation newborn female born to a 21 year old mother diagnosed with a right abdominal cyst (2.5 × 6.5cm) on prenatal ultrasound at 33 weeks gestation. She was delivered vaginally without complications. CT of the abdomen at the referring facility showed a right abdominal cyst (3.8 × 3.1cm) near the liver and kidney with free fluid in the right adenexal area. On admission to the Children's Hospital on day of life two, the infant was noted to have a full appearing, soft abdomen with good bowel sounds and no palpable mass appreciated. She had a quantitative HCG of 13.2 mIU/ml and AFPTM >36,300 ng/ml. Otherwise, her examination and laboratory studies were within normal limits. Abdominal ultrasound revealed good blood flow in the surrounding vessels and MRI showed a well defined, mostly high intensity, non-enhancing right lower quadrant mass with a cystic component. The differential diagnosis includes: congenital ovarian cyst, lymphangioma, mesenteric cyst, intestinal duplication cyst, meconium pseudocyst, hydro-metrocolpos, urachal cyst, bowel atresia/obstruction, renal cyst, and anterior meningocele. Surgical pathology revealed ovarian torsion on the right with giant hydatid/peritubal cyst formation (4.5 × 3.5 × 2.0cm) with evidence of cystic rupture, hemorrhage, and adhesions. She had an uneventful recovery and was soon discharged.

Conclusions: While congenital ovarian cysts were once considered uncommon, the increased use of ultrasound has led to increased detection. They are the most common abdominal tumor in female neonates. Small cysts (<0.9cm) are seen in 82% and larger macrocysts (>0.9cm) are seen in 30–34% of this population. They are usually unilateral and thought to be due to disordered folliculogenesis. Over 50% will resolve spontaneously and clinically significant cysts are rare. Torsion is the most common complication (40%) followed by infarction and cyst rupture. Most complicated cysts, like that in our patient, will require surgical intervention. However, aspiration can be used to decrease cyst size and limit complications.

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A NEW FORM OF EPICARDIAL PACING UTILIZING BIPOLAR SCREW-IN LEADS

KB. Ardoin ¹Tulane University Hospital, New Orleans, LA and ²Ochsner Clinic Foundation, New Orleans, LA.

Purpose of Study: The purpose of this study was to evaluate a new bipolar epicardial screw-in pacing lead reported to offer better sensing and pacing performance.

Methods Used: After IRB approval, the surgical data base was utilized to identify patients who had undergone implantation of a St Jude Medical Enpath Myopore Bipolar epicardial lead. Data collected included, indication for pacing, sensitivity, thresholds, impedance and complications. Data points were split into four categories: day 0, < one month, 1-3 months and > 3 months post implant.

Summary of Results: The Enpath Myopore Bipolar lead was implanted in 8 patients. There were three atrial (A) leads and seven ventricular (Ven) leads. With regard to the A lead, its acute threshold was 1.0 Volt (V) @ pulse width (pw) of 0.5 milliseconds (ms), current was 2.7 mA and impedance of 541 ohms. Follow-up for the three A leads revealed no significant change in threshold, current and impedance. The acute Ven threshold was 1.48 V @ pw of 0.5ms, current of 5.2 mA and impedance of 780 ohms. Follow-up revealed: One with a decrease, (1.4 V to 1.0 V), and three with increase V thresholds (1.7 V to 2.5 V). There was no significant change in sensing/ current or impedance during follow-up. There are no failed leads or complications.

Conclusions: This new bipolar epicardial lead appears to be effective for pacing patients. In short term follow-up, the lead performed satisfactory at pacing and sensing. Further follow up is needed to evaluate the long term success of this lead.

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HERPES SIMPLEX TYPE 1 CROUP WITH MENINGITIS

PH. Dahm, M. Mancao, F. Silver *USA Children's and Women's Hospital, Mobile, AL.*

Case Report: Introduction: Croup is an acute infectious illness commonly associated with parainfluenza and influenza virus infections. Herpetic croup is rare in occurrence and it is usually associated with prolonged use of steroids or observed in immunocompromised hosts. We therefore report a case of HSV-1 croup associated with meningitis and disseminated HSV disease in an immunocompetent child.

Case Report: A 12-month, male child was re-admitted to our institution for respiratory distress. He had been previously admitted one day prior to admission for barking cough, nasal congestion and increased respiratory stridor; he was diagnosed with croup, started on steroids and discharged home. Later in the day, he was readmitted due to severe respiratory distress. He was admitted to the Pediatric Intensive Care Unit, where he was intubated and ventilated and again started on steroids. Due to his worsening respiratory status, he underwent microlaryngoscopy and bronchoscopy; it demonstrated medial true vocal cord and subglottic edema with greater than 95% obstruction. Bacterial and viral cultures of the tracheal fluid were obtained. The tracheal viral culture yielded HSV-1 while the bacterial culture yielded *Staphylococcus epidermidis*. Cerebrospinal fluid (CSF) analysis was performed which revealed white blood cell count of 0 cells/uL, red blood cell count of 470 cells/uL, protein of 45 mg/dL, and glucose of 67 mg/dL. The HSV DNA by polymerase chain reaction (PCR) on CSF was positive for HSV. At this time, oral steroids were discontinued. HSV DNA by PCR was also detected in the serum sample obtained on admission. The patient was treated with 21 days of intravenous acyclovir and his immune work-up was normal. His respiratory status gradually improved and he was extubated. He was discharged home on oral acyclovir for 6 months.

Conclusions: This case illustrates the need to consider HSV as a cause for infectious croup, especially for patients who are severely ill or those patients with persistent respiratory compromise. It also important to recognize that aside from herpetic croup, patients may also present with HSV meningitis and disseminated HSV disease. Meningitis in the setting of herpetic croup can be easily missed, especially if the patient does not present with meningeal signs or symptoms.

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A NEONATE WITH CLINICALLY SIGNIFICANT COMPLICATED CONGENITAL OVARIAN CYST

W. Cline *University of Oklahoma HSC, Oklahoma City, OK.*

Case Report: Purpose of Study: To review the rare diagnosis of a clinically significant congenital ovarian cyst.

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ACUTE HEPATITIS DUE TO DILATED CARDIOMYOPATHY IN AN AIDS PATIENTVS. Dariya, A. Aravantagi, L. Scott *LSUHSC, Shreveport, LA.*

Case Report: Cardiac involvement with HIV infection has been well documented. Dilated cardiomyopathy (DCM) may be seen in patients with CD4 count <400. While the advent of Highly Active Anti-Retroviral Therapy (HAART) has significantly reduced the incidence of HIV associated cardiomyopathy, recent studies have indicated Azidothymidine (AZT) as one of the risk factors. DCM and subsequent Congestive Heart Failure (CHF) commonly manifests as shortness of breath, pedal edema and palpitations but rarely as acute hepatitis.

We present a 16-year-old African American female with past history of HIV nephropathy who presented with vague abdominal pain and nausea for four days. A year ago, she was started on HAART regimen and hemodialysis, but was non-compliant with both. Physical examination, on admission revealed tachycardia with a gallop, right upper quadrant tenderness and hepatomegaly. Labs revealed CD4 count of 43/mm³, HIV RNA viral load of 33,667 copies/ml, BUN of 82, creatinine of 10.6 and markedly elevated liver enzymes with AST and ALT levels of 1436 and 1080 respectively. Serology for Hepatitis A, B & C, Histoplasma, CMV, Mycoplasma and EBV was negative. Chest X-ray showed significant cardiomegaly, a new finding from a year ago. 2D Echo showed severe dilated cardiomyopathy with an ejection fraction of 5-10% and minimal pericardial effusion. The patient's BNP was >5000. Consequently, we reached a diagnosis of hypoxic hepatitis secondary to dilated cardiomyopathy and congestive heart failure. Urgent treatment was initiated with inotropic support and hemodialysis. AZT was discontinued once the diagnosis was confirmed. With improved control of her cardiac and renal function liver function tests (LFT) returned to baseline within 6 days. However, the patient continued to need inotropic support.

The differential diagnosis of liver abnormalities in HIV is broad. While viral and drug induced hepatitis are among the most common entities, it is prudent to search for other causes, especially in patients with significant comorbidities. Passive hepatic congestion is commonly seen in CHF and is associated with moderate elevation of aminotransferases, however, as this case illustrates severe new onset uncompensated DCM can cause significant hepatic injury characterized by very high LFTs.

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DETECTION OF PROSTHETIC MITRAL VALVE DYSFUNCTION USING EXERCISE ECHOCARDIOGRAPHY AND INTRACARDIAC PACINGW. Davis, W. Lutin *Medical College of Georgia, Augusta, GA.*

Purpose of Study: Children rarely require prosthetic mitral valves compared to adults. However, due to congenital or acquired heart disease, or complications from cardiac surgery, some children have mechanical mitral valves. Because of active growth, children will require prosthetic mitral valve replacement. Assessment of prosthetic mitral valve stenosis can be difficult. Resting Doppler gradients may not predict the severity of mitral valve stenosis during physical activity. The purpose of this study was to assess prosthetic mitral valve function during rest, exercise, and intracardiac pacing. Our hypothesis was that subtle abnormalities of mitral valve function could be detected during exercise or intracardiac pacing that was not found at rest.

Methods Used: Three patients with resting and exercise echocardiography, and intracardiac pacing during cardiac catheterization were compared.

Summary of Results: We found, compared to rest, exercise echocardiography demonstrated an increase in the transmittal gradient by 15%. Catheterization data demonstrated an average increase in pulmonary capillary wedge pressure from 13.6 mmHg to 19.3 mmHg; an average decrease in left ventricular end diastolic pressure from 12.3 mmHg to 2 mmHg; an average increase in the mean transmittal gradient from 6–16.6 mmHg; a decrease in systemic cardiac output by 25%.

Conclusions: We conclude that abnormalities in prosthetic mitral valve function occur with exercise or pacing before they can be detected by resting echocardiography. These modalities may assist with timing of surgical intervention.

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SPRAY IT WITH CAUTION: PRECOCIOUS PUBERTY FROM MATERNAL TRANSDERMAL ESTRADIOL SPRAYR. Gupta¹, K. Patra¹, V. Dariya¹, S. Sankararaman¹, S. Reddy^{2,1}, R. McVie^{2,1}¹Louisiana State University Health Sciences Center, Shreveport, LA and ²Louisiana State University Health Sciences Center, Shreveport, LA.

Case Report: A 3 year old girl and a 6 year old girl were referred to pediatric endocrinology clinic for precocious puberty. Both patients had enlarged breasts, advanced bone age, sparse pubic hair, accelerated growth rate and a uterine volume at the upper end of normal for age. The 3 year old girl had breast tissue at Tanner III, pubic hair at Tanner II, elevated serum estradiol level and pre-pubertal levels of follicle stimulating hormone (FSH) and leuteinizing hormone (LH). The 6 year old girl had breast tissue and pubic hair at Tanner II stage, vaginal discharge along with an elevated serum estradiol level. Gonadotropin releasing hormone (GnRH) stimulation test suggested gonadotropin independent precocious puberty (GIPP) for both the patients. No endogenous source for elevated estradiol level was identified on investigation for both the girls. Extensive family and social history revealed one common factor amongst these two distinct cases, both patients' mothers had recently undergone hysterectomy and were using a transdermal estradiol spray. The girls had breast budding within two months after the exposure thus making it highly probable that the source of elevated estradiol in both the patients is secondary to transmission from maternal estradiol spray. The exact mechanisms for transfer are not certain, however the studies done with respect to transfer to controls were done using adult population and fails to take into account the sensitivity of extremely low doses of estrogen to prepubertal children. Even minute amounts of exogenous estradiol can induce puberty in prepubertal children secondary to heightened response to sex steroids. Only a few cases have been reported regarding spread of estradiol through the use of transdermal formulations resulting in precocious puberty. The two cases presented here emphasize the importance of vigilant history taking with regards to exploring the possibility of exposure to exogenous estrogen in patients with GIPP. Identification and removal of the source will result in resolution of secondary sexual characters and prevent potential risks associated with premature sexual development.

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BEWARE OF TICKS! DIMINISHING PLATELETS, PERSISTENT PROLONGED COAGULATION STUDIESJ. Jones, D. Macariola *East Tennessee State University, Johnson City, TN.*

Case Report: 2 year old female presented with fever up to 105F associated with rash. These rashes initially appeared on her legs later becoming generalized. Admitted to outlying hospital and was treated with IV clindamycin and ceftriaxone. Despite antibiotic treatment the fever persisted, prompting referral to our facility. Her mother later on reported that she had a tick bite earlier in the week. Her immunizations were up to date.

She was irritable with temperature at 99.4 F, heart rate 152/minute & respiratory rate, 28/minute. Generalized petechiae and edema were noted but no nuchal rigidity.

WBC of 4,900, hematocrit of 24%, platelet count at 43,000 with differential count of neutrophils of 63%, lymphocytes 23% and bands 14%. Na 134 (low), Ca 8 (low), PT & PTT were prolonged with increased D dimer. CSF -low glucose, high protein and pleocytosis with predominance of PMN. Albumin levels & platelets were low for days.

Admitted to ICU and received oxygen and IV fluids. Doxycycline was added to ceftriaxone for her antibiotic treatment. She was treated with furosemide and albumin for pulmonary edema. Diagnosed to have DIC & anemia and was given multiple fresh frozen plasma, platelets & packed RBC. R. rickettsii IgM & IgG titers were elevated at 1:64 & 1:512, respectively. She gradually improved and was discharged home with oral doxycycline.

Rocky Mountain Spotted Fever (RMSF) is caused by *Rickettsia rickettsii*. It is the most common fatal tick-borne disease in the United States. Typically, it presents as fever, myalgias, headache, and petechial rash. It can cause damage to the endothelium of any organ resulting in increased vascular permeability, edema, hypovolemia, and hypotension. Sometimes, life-threatening consequences of vascular injury in the CNS and lung such as meningoencephalitis and pulmonary edema can occur as presented in our

patient. Our case is unique because it illustrates that DIC may develop as complication of RMSF. Clinicians should therefore be aware of this complication so that appropriate interventions can be done in timely manner to prevent mortality and morbidity.

198**CORNER OF THE MIND**

AD. Lowery¹, R. Smalligan² ¹*East Tennessee State University, Johnson City, TN* and ²*TTUHSC, Amarillo, TX.*

Case Report: A 2-month-old boy presented with 2 weeks of cough, fussiness, fevers and periods of inconsolable crying. He had no sick contacts or foreign travel and pregnancy had been uncomplicated. No meds. No family history of neurologic or genetic disorders. PE: irritable; lungs and heart normal, abdomen: nontender mass 5cm below the LCM, skin: scattered petechiae; hypospadias, neurologic exam: nonfocal. Lab: Hgb 12.3, WBC 19.3, platelets 20,000, LDH 1060 (nl 180–430 U/L), AST 441, and ALT 120. Abd US: hepatosplenomegaly. Bone marrow biopsy consistent with consumption. On the 3rd day the patient developed seizures. Head CT: areas of hyperdensity in R frontal lobe. LP: lymphocytosis with negative cultures. The EEG had epileptiform discharges in the right frontotemporal region. MRI: multiple focal areas of meningeal enhancement consistent with encephalomalacia. TORCH titers were negative except for elevated toxoplasmosis IgG though fundoscopic exam was normal. He was initially treated for presumed congenital toxoplasmosis. This was stopped when the Sabin Feldman dye test excluded the infection. Efforts were continued to determine the etiology of the patient's ongoing multi-system dysfunction including a negative genetics work-up. Ultimately, CSF was re-obtained and sent for INF-alpha levels which returned elevated, confirming the diagnosis of Aicardi-goutieres syndrome.

Discussion: First described in 1984 by Jean Aicardi and Francois Goutieres, Aicardi-goutieres syndrome (AGS) is a rare, autosomal recessive, progressive encephalopathy that presents during the first year of life. Parents often bring affected children at 4–12 months of age to their pediatrician with complaints of irritability, feeding difficulties, unexplained febrile episodes, or seizures. Our patient had these features along with hepatosplenomegaly, elevated transaminases, anemia, and thrombocytopenia. These findings can mimic a congenital infection which must be excluded as was done. Other typical features of AGS include acquired microcephaly, basal ganglia calcifications, white matter abnormalities, chilblain-like lesions, CSF lymphocytosis and the hallmark finding of increased CSF INF-alpha. Though rare, pediatricians need to be aware of AGS and keep it in the differential diagnosis for children with new-onset neurologic and hematologic abnormalities.

199**A COUGH THAT BECOMES AN EMERGENCY**

D. Macariola, J. Jones *ETSU, Johnson City, TN.*

Case Report: Objective: To increase awareness among clinicians about non-traumatic spontaneous splenic rupture as complication of EBV infection.

17 year old male who presented with sore throat associated with cough and fever. Diagnosed to have a streptococcal pharyngitis and treated with oral azithromycin. On follow up he was found to have splenomegaly. He later developed a sudden onset of severe abdominal pain immediately following a coughing episode. No history of trauma.

PE findings were pertinent for heart rate of 135/minute, pallor of skin and conjunctivae, abdominal distention and profound tenderness on the left upper quadrant.

Pertinent Labs: Initial hemoglobin and hematocrit were 15 gm/dl and 41 % respectively dropping to 11 gm/dl and 30% in 1 hour. CT abdomen revealed fluid collection around the spleen. His Monospot test was positive. EBV Viral capsid antigen IgM and IgG titers were elevated while CMP was normal. His total WBC count during the first post op day was 26,000.

Hospital Course: He received pneumococcal and meningococcal vaccines pre-op and had emergency laparotomy and splenectomy for splenic rupture. Twenty four hours post surgery he developed fever with leucocytosis and was treated with 7 day course of IV ceftriaxone. No bacteria were isolated from blood and urine cultures. He was discharged home improved with oral penicillin prophylaxis.

Discussion: Splenomegaly can occur in 50% of children infected with EBV. Each time there is splenomegaly, there is a risk of splenic rupture. Most of the time splenic rupture in EBV infection is associated with trauma. Our case

illustrates that splenic rupture can occur even without trauma. It was spontaneously induced by a coughing episode. Splenic rupture is an emergency. Surgical intervention should be done in timely manner to prevent intra-abdominal blood loss. Prior to splenectomy, children should receive pneumococcal and meningococcal vaccines to prevent future pneumococcal and meningococcal sepsis. In addition, providing daily penicillin treatment to splenectomized children will also prevent pneumococcal sepsis. Clinicians should recognize that coughing, a normal body reflex may induce splenic rupture in children with splenomegaly due to EBV infection as depicted in our case.

200**UROFACIAL (OCHOA) SYNDROME**

PN. Madonia, D. Kurepa, C. Pant, V. Kakkilaya, H. Chen *Louisiana State University - Shreveport, Shreveport, LA.*

Case Report: A 7 year old Caucasian girl was admitted with a chief complaint of abdominal pain for 10 weeks duration. She had episodes of intermittent nausea and vomiting and weight loss. Prior history included some developmental delay and enuresis with delayed toilet training. Physical exam revealed an abnormal facial expression when smiling and a CT scan of the abdomen revealed bilateral hydronephrosis. Laboratory analysis including stool studies and cultures were all normal. Non obstructive hydronephrosis was confirmed by a nuclear scan and a cystourethrogram showed no evidence of vesicoureteral reflux. EGD was normal and colonoscopy showed a benign juvenile polyp. The nausea and vomiting subsided with conservative management. A diagnosis of Ochoa syndrome was made due to the abnormal facial expression and the bilateral non-obstructive hydronephrosis. The urofacial syndrome, also known as Ochoa syndrome is an extremely rare genetic disorder named after Colombian physician Bernardo Ochoa, who first studied the disorder in a small population of Colombian children. Beginning in 1965, Ochoa noted several children who displayed symptoms of a neurogenic bladder, together with a peculiar facial expression described as an “inverted smile”. Since then, there have been about 100 cases documented from various parts of the world. Today, the urofacial syndrome is known to consist of three main components; a neurogenic bladder, the specific facial expression of an “inverted smile,” and a pattern of autosomal recessive inheritance. Every patient diagnosed with Ochoa syndrome has had symptoms of a neurogenic bladder. This bladder dysfunction can cause problems that begin mild and if left untreated, progress to severe bladder disease and renal failure. Some patients complain of constipation and fecal soiling in addition to the urinary problems, a fact that has led some researchers to propose the term ‘dysfunctional elimination’ to describe the 2symptomatology of these patients. The facial abnormality of Ochoa syndrome is a characteristic facial expression that is described as a “facial grimace” while smiling. This grimace is highly diagnostic of Ochoa syndrome and recognition of this feature is paramount for a clinician to make a diagnosis.

201**GRISSEL'S SYNDROME: SUBLUXATION OF THE CERVICAL SPINE ASSOCIATED WITH STREPTOCOCCAL PHARYNGITIS**

D. Moya, L. Crews, K. Tramell *University of South Alabama, Mobile, AL.*

Case Report: A two year old male presented with an acute onset of severe torticollis associated with fever for one day and decreased oral intake. The family denied any history of trauma. Physical exam findings a few hours after the onset of left-sided torticollis revealed a toddler in mild distress associated with notable left-sided and posterior neck edema with minimal tenderness. Additional pertinent physical findings included a mildly erythematous oropharynx without exudates or significant tonsillar hypertrophy. The primary care provider performed a rapid streptococcal antigen detection test which was negative, a CBC which revealed an elevated WBC of 25,000 with a left shift, and lateral neck X-rays which demonstrated C1–C2 subluxation and prevertebral edema with suspicion for retropharyngeal abscess or hematoma. Decision was made to perform a CT scan of the neck with and without contrast which revealed a 1.2 × 1.3 cm non-enhancing low attenuous parapharyngeal abscess and subluxation of C1–C2. Additional history did reveal a contact who had treatment for Streptococcal pharyngitis two weeks prior. The patient was admitted to the pediatric intensive care unit and IV antibiotics were administered until incision and drainage of the

abscess by ENT occurred. The patient also had a C-collar placed and was followed by neurosurgery. Two days after admission, the throat culture revealed Group A Streptococcal infection. Discussion: Grisel's syndrome is subluxation of C1 on C2 associated with an infectious condition in the head or neck. It is felt that there is a peridontoidal vascular plexus that provides drainage for the posterior superior pharyngeal region. Since there is not lymphoglandular tissue in this plexus, hematogenous spread of septic exudates from the pharynx can be transferred to the C1–C2 space resulting in subluxation of the atlantoaxial joint as a result of inflammation to the transverse and facet capsular ligaments. Treatment of the infectious process with stabilization of the subluxation to provide ligamentous healing is the priority. Prolonged immobilization for six to eight weeks with the potential need for posterior atlantoaxial arthrodesis is necessary.

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UTILITY OF CHILDHOOD GLUCOSE HOMEOSTASIS VARIABLES IN PREDICTING ADULT DIABETES AND RELATED CARDIOMETABOLIC RISK FACTORS: THE BOGALUSA HEART STUDY

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Purpose of Study: This study sought to examine the usefulness of childhood glucose homeostasis variables (glucose, insulin, and insulin resistance index (HOMA-IR)) in predicting pre-diabetes and type 2 diabetes, and related cardiometabolic risk factors in adulthood.

Methods Used: This retrospective cohort study consisted of normoglycemic (n=1058), pre-diabetic (n=37), and type 2 diabetic (n=25) adults aged 19-39 years who were followed on average for 17 years since childhood.

Summary of Results: At least 50% of the individuals who ranked highest (top quintile) in childhood for glucose homeostasis variables maintained their high rank by being above the 60th percentile in adulthood. In a multivariate model, the best predictors of adulthood glucose homeostasis variables were the change in body mass index (BMI) from childhood to adulthood and childhood BMI, followed by the corresponding childhood levels of glucose, insulin, and HOMA-IR. Further, children in the top decile vs the rest for insulin and HOMA-IR were 3.2 and 2.9 times, respectively, more likely to develop pre-diabetes; children in the top decile vs the rest for glucose, insulin, and HOMA-IR were 2.9, 3.4, and 3.4 times, respectively, more likely to develop diabetes, independent of change in BMI, baseline BMI, and total cholesterol/high-density lipoprotein cholesterol ratio. In addition, children with adverse levels (top quartile vs the rest) of glucose homeostasis variables displayed significantly higher prevalences of, among others, hyperglycemia, triglyceridemia, hypertension, and metabolic syndrome.

Conclusions: Adverse levels of glucose homeostasis variables in childhood not only persist into adulthood but also predict adult pre-diabetes and type 2 diabetes and relate to cardiometabolic risk factors.

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DIGEORGE ANOMALY, AN ELUSIVE 'FISH' TO 'CATCH': A CASE REPORT

KP. Patra¹, R. Gupta¹, T. Milligan², M. Lowery- Nordberg¹ ¹LSUHSC, Shreveport, LA and ²Driscoll Children's Hospital, Corpus Christi, TX.

Case Report: A complete DiGeorge anomaly (DGA) consists of a constellation of congenital cardiac defects, dysmorphic facies, hypocalcemia and immunodeficiency. A term male neonate, with unremarkable family history, was born via normal vaginal delivery. There was no history of maternal diabetes or teratogenic exposure. Examination showed dysmorphic facies with low set ears, micrognathia, epicanthic folds, broad nasal bridge, choanal stenosis and right sided facial palsy. Cardiac auscultation revealed a 3/6 holosystolic murmur heard along the left sternal border. Echocardiogram showed double outlet right ventricle, large ventricular septal defect and a large patent ductus arteriosus. He developed hypocalcemic seizures and was initiated on calcium, magnesium and vitamin D supplementation. Serum parathormone level was low. Patient underwent pulmonary artery banding and ductal ligation on Day 7 of life. Thymus and parathyroid glands were noted to be absent during surgery. Flow cytometry showed T-cell lymphopenia. Fluorescence in-situ hybridization (FISH) studies for chromosome 22q11 and 10p14 microdeletions were normal. Oligonucleotide comparative genomic hybridization showed no diagnostic copy number changes. We can only hypothesize the etiology in our case. DGA is a dysembryonic

field defect involving the third and fourth pharyngeal pouches and is attributed to genetic or environmental perturbation in neural crest migration. It has markedly variable penetrance and expressivity. 22q11.2 microdeletion is seen in around 90% cases. It is a 3-Mb region comprising of at least 30 genes. Other chromosomes have also been implicated. Maternal diabetes, retinoic acid and fetal alcohol embryopathy can also result in a similar syndrome. None of the investigated genes has been shown unequivocally to explain the phenotype completely. The expression of these genes, in turn is dynamically regulated by modifiers which are located at a distance. We speculate that in FISH-negative patients, DGA phenotype can result from an aberration or mutation of any of these diverse genes or their modifiers. Unraveling this complex cardiac embryogenesis will have implications in management and genetic counseling.

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THE MANAGEMENT OF MULTIFOCAL ATRIAL TACHYCARDIA IN THE NEWBORN WITH ENTEROVIRUS MYOCARDITIS

DH. Petroni¹, C. Snyder², MR. Recto¹, S. Yang¹ ¹Tulane University School of Medicine, New Orleans, LA and ²Ochsner Health System, New Orleans, LA.

Case Report: Multifocal atrial tachycardia (MAT) is a rare arrhythmia that can present in the neonate. The etiology of MAT is varied and may be secondary to myocarditis. Management of myocarditis related arrhythmias in the neonate is challenging due to the lack of an evidence based standard for its diagnosis and treatment. We report a newborn with MAT secondary to enterovirus myocarditis. Our patient was a 7 day-old, near 38 week gestational age male who was transferred to our center after development of intractable tachycardia that was resistant to adenosine therapy. On our workup, his electrocardiogram showed varying p-wave morphology, irregular P-P intervals and a rapid ventricular rate; a diagnosis of MAT was made. Echocardiography elucidated both normal cardiac anatomy and coronary arteries with normal biventricular systolic function. The patient was started on Esmolol intravenous (IV) infusion; the dose was titrated. But his tachycardia was poorly controlled. Amiodarone 15mg/kg/day IV infusion was then added to his treatment regimen, but again, his tachycardia was not adequately controlled. On retrospective review of the patient's history, it was found that he had a low grade fever (38.3°C) prior to his admission to the local hospital. The patient was then treated for a presumptive viral myocarditis with IV immunoglobulin. The patient's cardiac output was supported with an IV infusion of Milrinone, Dopamine and calcium chloride. Flecainide (80mg/m²/day in 3 divided doses PO) was also initiated. On the 6th day of his treatment, he converted to a sinus rhythm with a heart rate of 120–140bpm and 1st degree heart block. During the course of treatment, viral PCR panels returned a positive result for enterovirus. Most recent echocardiogram revealed normal left ventricular systolic function and mild mitral valve regurgitation. Atrial arrhythmias with enterovirus myocarditis have been reported with associated atrial dilatation and ventricular diastolic dysfunction. It is possible that persistent arrhythmia and resistance to treatment was secondary to persistent viremia and myocardial damage. Therefore, a high index of suspicion and prompt, appropriate intervention are crucial for the management of neonatal MAT with viral myocarditis.

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WISH IT WAS THE FISH!

R. Philip, G. Abraham, M. Lucas *East Tennessee State University, Johnson City, TN.*

Case Report: CASE HISTORY: A 2.5 y/o previously healthy female presented to the ER with a history of vomiting, wheeze, truncal rash and increasing severity of excessive itching. While at a friends' home for a birthday party, the mother reported a history of ingestion of fresh fish (mahi mahi) sometime prior to the appearance of the above symptoms. There was no history of being left unattended, having access to any medications/drugs or being bitten by any insect. PMH: no history of asthma, hospitalizations or food allergies SH: lives with the mother. No h/o similar symptoms in anyone else who consumed the fish. P/E: Well appearing, though drowsy. VS: T 98.4F HR: 100/min BP: 90/50 RR: 44/min SaO₂ 91% in R.A. HEENT: slowly reactive 5mm pupils BS: b/l expiratory wheeze Skin: urticarial pruritic rash primarily truncal. Remainder of exam normal. With the history of fish consumption and histamine related signs and symptoms, an initial impression of Scombroid fish poisoning was made and the child was treated with an antihistamine, albuterol and supplementary oxygen to keep his SaO₂ > 92 %

with clinical improvement; drowsiness persisted. Further workup included a Chest Xray, CBC with differential count and a CMP which were normal. Histamine levels pending. The urine drug screen was positive for opioids and subsequent investigation into the history revealed maternal history of chronic codeine use with easy access to codeine containing medications at home. CPS was notified.

This case exemplifies the importance of not only taking a good history but also recognizing red flags when there are inconsistencies in the history and clinical exam. It highlights the usefulness of a urine drug screen in any child with questionable transient drowsiness. Clinicians should recognize the less common side effects of opioid ingestion like histamine release related urticaria, pruritis and bronchospasm. This could well have been scombroid fish poisoning, which is an acute syndrome resulting from consumption of fish containing high levels of histamine. The symptomatic treatments of both conditions are the same. However, clinicians must keep in mind that not all cases of opioid ingestion have classic pin point pupils and respiratory depression; some opioids destabilize mast cells in a dose-dependent fashion, causing histamine release which mimics an "allergic reaction".

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UNUSUAL CLINICAL MANIFESTATIONS AND COMPLICATIONS OF CARDIOMYOPATHY IN CHILDREN

U. Ponniah, K. Ward, M. Paliotta, C. Sperrazza, S. Baker, A. Shah, E. Overholt *Oklahoma University Health Science Center, Oklahoma City, OK.*

Purpose of Study: 1.To assess the treatable causes of Dilated Cardiomyopathy like severe Coarctation of the Aorta, Anomalous Left Coronary Artery from the left Pulmonary Artery (ALCAPA) and Arrhythmia.

2.To understand the unusual manifestations and complications of Cardiomyopathy in children.

Methods Used: Case series, retrospective study.

Summary of Results: Nine patients had unusual manifestations related to cardiomyopathy of the cases of Cardiomyopathy we recently reviewed. Two patients (both infants) had presented with malignant recalcitrant ventricular tachycardia secondary to a rare, LV non-compaction type of cardiomyopathy; one patient expired and the other underwent cardiac transplantation.

Three patients had coronary artery abnormalities resulting in dilated cardiomyopathy. Two of these patients had ALCAPA resulting in dilated cardiomyopathy; both underwent successful surgical repair, however one of them died suddenly several weeks later and the other had an Implantable Cardiac Defibrillator. The third patient with coronary artery abnormality had presented with dilated cardiomyopathy due to total occlusion of left main coronary artery long after a sub aortic stenosis resection and this patient died suddenly while the evaluation was ongoing for a possible re-canalization procedure. One patient (infant) with hypertrophic cardiomyopathy developed severe restrictive physiology and underwent cardiac transplantation. Three patients were noted to have LV thrombus associated with myocarditis / cardiomyopathy which resolved after Lovenox therapy. Of the patients with LV thrombus, an 8 year old girl developed a large LV thrombus secondary to significant dilated cardiomyopathy due to severe coarctation of the upper thoracic aorta. To the best of our understanding this is the first reported case of such an unusual combination.

Conclusions: Treatable causes of dilated cardiomyopathy needs to be carefully looked for as the prognosis is dependent on the prompt identification and treatment of the underlying problem. Ventricular tachycardia, LV thrombi and sudden death are some of the unusual manifestations and complications secondary to cardiomyopathy in children. Primary care providers need to be aware of these presentations and management.

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FLU BROUGHT OUT THE DIAGNOSIS - INFLAMMATORY MYOFIBROBLASTIC TUMOR OF THE LUNG IN A CHILD

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Case Report: We report a five year old boy who initially presented with influenza A and secondary mycoplasma pneumonia. X-ray taken to evaluate his pneumonia revealed a homogenous opacification of the left lung base. Ultrasound and CT scan confirmed the presence of 6 × 5 × 5 cm homogenous solid mass in the posterior part of the left lung base. There was no pleural

effusion or hilar lymphadenopathy. The mass had neither calcification nor fluid in it. X-ray taken three years prior did not show this mass. He was otherwise asymptomatic during this interval. Laboratory investigations revealed anemia, thrombocytosis, high ESR and CRP in favour of an ongoing chronic inflammatory process. Blood culture and PPD were negative. Serology and culture for histoplasmosis were negative as well. The tumor was removed by open thoracotomy and specimen subjected for histopathology. Gross pathology revealed a firm mass without necrosis and tightly adherent to the overlying lung parenchyma. Frozen section revealed the presence of spindle cells with chronic inflammation in favour of inflammatory myofibroblastic tumor (IMT) of the lung. Resection margin was clear without tumor cells. Immunohistochemistry was positive for anaplastic lymphoma kinase 1 (ALK1), vimentin and smooth muscle actin and also negative for pancytokeratin and CD 34. This staining pattern correlates with IMT and further confirmed the connective tissue origin of the tumor. IMT is an uncommon mesenchymal neoplasm of children and young adults occurring most commonly in the lungs, abdominal cavity and retroperitoneum. The most common presentation is incidental detection of mass by chest radiography. It is still unclear whether IMTs represent a primary inflammatory process or a low-grade malignancy with a prominent inflammatory response. Complete surgical excision is curative in majority of the tumors. Both local recurrence and distant metastasis have been reported, in some cases, secondary to incomplete resection. Complete resection with long term follow up is recommended.

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CRICOID CALCIFICATION MIMICKING A FOREIGN BODY IN THE AIRWAY IN A CHILD

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Case Report: Ossification of laryngeal cartilages, which is often described as a degenerative process in hyaline cartilage, usually begins after the skeletal growth is otherwise complete at 20-22 years of age. The vertical ossification of the cricoid lamina can be misdiagnosed as a foreign body in the airway.

We present an 18 year old previously healthy Caucasian female, who came to the emergency department with fever, sore throat, difficulty in swallowing, cough, neck pain and neck stiffness for the last 2 days. On physical exam she had evidence of bacterial pharyngitis with pus on the right tonsil and posterior pharynx hyperemia. Due to the severity of the presenting symptoms, AP and lateral neck X Rays were obtained. These revealed an irregular 2 cm long vertical opacification posterior to the airway. The patient was started on conservative treatment including pain management and antibiotics. After a normal flexible laryngoscopy, flexible bronchoscopy was performed to rule out a foreign body versus a calcified mucus concretion due to bacterial tracheitis. Bronchoscopy did not reveal any foreign body and showed only mild erythema of the tracheal mucosa. Upon review of the neck x-rays by another Radiologist, the irregular calcification was identified as an incidental calcification of the cricoid cartilage.

There are only a few cases reported of cricoid calcification all above the ages of 40-50 years. In each of these cases the presentation was similar with esophageal or tracheal foreign body suspected the opacification was seen on plain films of the neck. This is the youngest case reported in the English literature we could find. Physicians who treat adolescents and young adults should be aware that the cricoids cartilage may calcify at least as early as 18 years of age.

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HOLT-ORAM SYNDROME: A NOVEL MUTATION IN THE TBX5 GENE WITH FINDINGS OF MULTIPLE VENTRICULAR SEPTAL DEFECTS

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Case Report: We report a patient with a novel mutation in the TBX5 gene who had multiple ventricular septal defects (VSDs) identified by prenatal and postnatal echocardiograms. The patient was born at 38 weeks gestation and was found to have first degree atrioventricular (AV) block and mild malformation on both of his thumbs. The patient was treated for congestive heart failure and underwent surgical repair of his multiple VSDs and tricuspid valvuloplasty at 3 months of age. The patient's family history is

significant for an autosomal dominant hand-heart syndrome going back 3 generations. The patient's mother had surgical repair of a secundum atrial septal defect and pacemaker insertion; she has bilateral brachydactyly and low, sloping shoulders.

Microarray CGH using an Agilent 44k chip on the patient was reported as normal. We then sent maternal blood to GeneDx for complete sequencing of the TBX5 gene, and a heterozygous duplication of 7 nucleotides was identified in exon 4 [GTGA{AGGTGAC}GGGCC]. The c.269_275dup7 mutation causes a frameshift starting with codon Leu94, changing it to Aspartic Acid, and creates a premature Stop codon at position 4 of the new reading frame, denoted p.Leu94AspfsX4. Targeted mutation testing in our patient was also positive for this novel mutation. Testing of other family members has not yet been done.

Holt-Oram syndrome (HOS) was first reported in 1960 and the TBX5 gene at 12q24 was identified in 1997. HOS is an autosomal dominant disorder with high penetrance and variable expressivity. Pathogenesis is believed to be due to haploinsufficiency. Both mutations in TBX5 and contiguous deletions including TBX5 have been reported. Patients with HOS have a triad of upper limb anomalies, cardiac defects and conduction disturbances. However, little is known for HOS patient with multiple VSDs (swisscheese-like ventricular septum defects). Appropriate genetic counseling and testing, prenatal identification of offspring at risk, and coordinated postnatal care of affected newborns is crucial for the patient's outcome.

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SPINAL EPIDURAL ABSCESS COMPLICATING CA-MRSA MENINGITIS

T. Yohannan¹, RT. Mohon² ¹East Tennessee State University, Johnson City, TN and ²East Tennessee State University/Quillen College of Medicine, Johnson City, TN.

Case Report: A 14 year old Caucasian male presented with 5 days of meningismus, headache, fever and vomiting. Several family members reported prior history of "boils" and "blisters". Physical exam: febrile, toxic appearing teenager with positive Kernig and Brudzinski signs but no other focal deficits. CSF was consistent with bacterial meningitis with wbc 8,400, glucose 38 and protein 87. Blood cultures grew MRSA. He was treated with vancomycin, gentamicin and rifampin based on bacterial sensitivities. After a week of clinical improvement, he worsened with a new fever and excruciating back pain with radiation to the lower extremities. Neuro exam revealed depressed knee and ankle DTR's. A contrast enhanced MRI of the spine showed a spinal epidural abscess (SEA) spanning the entire thoracic spine extending into the lower cervical and upper lumbar spine. The SEA displaced the spinal cord anteriorly. Multiple laminectomies were performed at T1-T2, T5-T6 and T9-T10 levels to debride the abscess. An epidural catheter was left in place till a follow up MRI showed resolution of the SEA. Abscess culture grew MRSA. The patient was discharged on 18th hospital day to complete a total 8 weeks of intravenous rifampin and linezolid.

Discussion: SEA is a rare clinical entity. Incidence is estimated to be 3 cases per 10,000 adults. SEA is unusual in the pediatric population with about 90 reported cases. Staphylococcus species is the common causative organism with MRSA accounting for up to 15%. SEA is commonly described in adults with diabetes, spinal abnormalities, IV drug abuse and malignancy. Virulent strains of community acquired-MRSA, (CA-MRSA) have been reported as causing SEA in previously healthy teenagers. Symptoms are described as a triad of fever, spinal pain and progressive neurological deficits. SEA should be suspected in any patient with this triad or an inadequate response to antibiotics. In our patient the SEA was confirmed by MRI with gadolinium contrast. Urgent decompressive laminectomy is recommended for patients with motor deficits and neurological deterioration with intravenous antibiotics for 6 to 8 weeks. A high index of suspicion and timely diagnosis are needed to effectively treat this uncommon but potentially disastrous clinical entity.

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A 5 WEEK OLD MALE PRESENTING WITH INFANTILE HYPERTROPHIC PYLORIC STENOSIS FOLLOWING AZITHROMYCIN THERAPY: A CASE REPORT

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Case Report: A relationship between oral erythromycin therapy and infantile hypertrophic pyloric stenosis was first suggested in the medical literature in 1976 (1). In 1999 the CDC acknowledged a causal relationship between oral erythromycin and infantile hypertrophic pyloric stenosis (2). Currently, this is accepted dogma among pediatricians and this potential risk is addressed with parents whenever erythromycin is recommended for a neonate.

To date there have not been any large scale studies to investigate the extent of infantile hypertrophic pyloric stenosis associated with oral erythromycin, azithromycin or other macrolides. This is the third report in the literature of infantile hypertrophic pyloric stenosis associated with azithromycin (3).

This case is a five week old white male born at 35 weeks of gestation who developed forceful episodes of emesis over the preceding 24 hours. At the time of presentation he was vomiting following each feed. At three weeks of age he had received five days of oral azithromycin for presumptive *Chlamydia* conjunctivitis and for prevention of pneumonia. An abdominal ultrasound confirmed pyloric stenosis and a successful pyloromyotomy was performed.

This case supports the idea of an association between oral azithromycin (and additional macrolides) and infantile hypertrophic pyloric stenosis. This potential risk should be considered when recommending azithromycin in the neonatal period until further studies in this arena are concluded.



Liver U/S exhibiting a clot in the left portal vein with obstruction of distal flow

Perinatal Medicine

Joint Poster Session

5:00 PM

Thursday, February 25, 2010

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A RARE YET NOTEWORTHY CASE OF CONGENITAL PORTAL VEIN THROMBOSIS (PVT) IN A TERM NEWBORN

G. Abraham, D. Shah ETSU, Johnson city, TN.

Case Report: A 39 weeks AGA male born to a 26 year old G5P4 by spontaneous vaginal delivery was transferred to NICU for persistent respiratory distress from an outlying facility. Prenatal history is positive for smoking and use of Buprenorphine for opiate dependence. Physical examination was unremarkable except for intercostal retractions, tachypnea and mild hepatomegaly. Initial chest x-ray was significant for small pneumothorax and RDS changes. Repeat chest x-rays revealed constant elevated right hemidiaphragm even after dissolution of small pneumothorax, prompting a fluoroscopy of diaphragm and abdominal U/S. The fluoroscopy showed normal diaphragm and the abdominal U/S revealed a clot in the left portal vein with absence of distal flow. D-dimer elevation at 1863ng/ml suggested a consumptive process. Hematology workup including tests for Coagulation screen, Peripheral smear, Protein C&S, hemoglobinopathies, and lipoprotein A levels were negative for clot etiology. Patient was treated with LMW heparin subcutaneously for 14 days. Serial U/S done during and end of medication showed resolution of clot establishing distal flow.

Discussion: PVT unrelated to catheters is rare in the newborn but when present can go undiagnosed with a consequence later in life of portal venous hypertension and GI Bleeding. Treatment with LMW Heparin in this patient

established distal flow and probably preventing the complications. This case alerts clinicians to identify liver pathology like PVT in neonates with an elevated right hemidiaphragm, even in the absence common etiologies like umbilical venous catheter or conditions like Asphyxia and Persistent pulmonary hypertension.

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NEONATAL CHYLOTHORAX: A 5-YEAR RETROSPECTIVE REVIEW

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Purpose of Study: To determine the etiology, clinical course, treatment modalities and variables affecting the outcome of newborns admitted to the neonatal intensive care unit at the University of Oklahoma in a five-year period.

Methods Used: The electronic medical records of newborns admitted to the neonatal intensive care unit, from January, 2003, to January, 2008, with a confirmed diagnosis of Chylothorax, were retrospectively retrieved and extensively analyzed.

Summary of Results: 9 newborns were identified with a confirmed diagnosis of chylothorax. 7 (78%) were male; 6(67%), preterm. Cardiac surgery (n=5) was the most common etiology. All patients were initially treated with conservative therapy (mean= 16 days). This modality of treatment resulted in resolution of chylothorax in 4 patients (44%). Surgery was performed in 3 patients who failed conservative management. 2 (67%) responded. Octreotide was given to 2 patients after conservative therapy failed. 1 (50%), responded.

The timing to drain the pleural effusion was greater in the cardiac surgery group (mean of 7 days) when compared with patients who did not have cardiac surgery (mean of 6). This association was not statistically significant (p=0.81). Thoracostomy tubes were placed in all patients. The mean number of days with a chest tube in place was 12 (2-62 days). The time needed to drain the effusion was found to have a negative correlation ($r = -0.767$) with APGAR score at one minute of life (p=0.0158). When analyzing variables across treatment group, we found that patients treated only with conservative therapy had a median APGAR score of 8 versus 5 in the non-conservative group (p=0.0442). Mortality occurred in one patient who failed conservative and non-conservative therapy.

Conclusions: Cardiac surgery is the most common cause of chylothorax among our patients.

Male babies born to term pregnancies were the most commonly affected.

Timing to drain the chylous effusion was negatively associated with APGAR scores at one minute of life (p=0.0158). Patients who responded to conservative therapy alone were found to have a higher APGAR score at one minute of life (p=0.0442).

Randomized controlled trials are needed to determine the efficacy of current therapies for the management of neonatal chylothorax.

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MORGANELLA MORGANII SEPSIS IN A PREMATURE NEONATE: A CASE REPORT

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Purpose of Study: *Morganella morganii* is a gram-negative bacillus that is part of normal gastrointestinal flora. It is commonly isolated from the urine of chronically catheterized adults and is known to cause infection in immunocompromised individuals. It has rarely been reported as a cause of neonatal sepsis.

Methods Used: Literature review.

Summary of Results: A 834 gram product of a 26 week gestation was delivered vaginally to a 30 year old primigravid woman. The pregnancy was complicated by preterm premature rupture of membranes for approximately 75 hours prior to delivery, maternal fever, and chorioamnionitis. The infant had poor respiratory effort and was immediately intubated. The patient had a large collection of purulent material overlying the vocal cords. A tracheal aspirate culture and a blood culture were collected and antibiotic therapy was initiated with ampicillin and gentamicin. Blood culture was positive in <24 hours for *Morganella morganii* and tracheal aspirate was positive for *Morganella morganii*, *Escherichia coli*, and *Proteus mirabilis*. Antimicrobial therapy was

changed to meropenem following identification of *Morganella*. A lumbar puncture was performed 6 days after birth and cerebrospinal fluid culture was negative. However, the CSF white blood cell count was 167 (nl 0-30) with 79% neutrophils (nl 0-8%) with 122,500 red blood cells. Due to concern for development of a brain abscess, a head ultrasound was performed and was unremarkable. The patient was treated with cefepime for 28 days following the first negative blood culture. Patient was discharged from the neonatal intensive care unit at 2 months of age with concurrent diagnoses of resolving grade I intraventricular hemorrhage, gastroesophageal reflux, anemia of prematurity and premature feeding.

Conclusions: This is one of the few reported cases of neonatal sepsis in a premature infant secondary to *Morganella morganii*, who has survived with little to no sequelae. *Morganella morganii* should be considered as a possible etiology of neonatal sepsis, especially if maternal chorioamnionitis present.

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NEWBORN STRIDOR AND RESPIRATORY DISTRESS: ANOTHER CASE FOR PARADOXICAL VOCAL CORD MOVEMENT

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Case Report: The most common cause of stridor in the neonatal period is laryngomalacia followed by bilateral vocal cord paralysis. We present a case of a term newborn male infant who presented with stridor immediately following a routine delivery by C-section; infant was intubated and required mechanical ventilation. Rigid bronchoscopy on day of life 1 did not demonstrate any vocal cord or upper airway anomalies. Physical exam except for stridor was normal. The infant failed extubation multiple times and underwent a flexible bronchoscopy on DOL 13, which demonstrated that the vocal cords adducted during inspiration, and abducted during expiration. Infant underwent a tracheostomy and was subsequently discharged home on a trach collar and feedings per os. Interestingly, upon detailed questioning, patient's father and older sibling reportedly had stridor at birth that resolved around 18 months of age. Our baby did undergo genetic testing, which demonstrated additional centromeric material on chromosome 15 which may represent a polymorphism. The family is in the process of undergoing genetic testing as well. This case, diagnosed, as paradoxical vocal cord movement is similar to another case reported in the literature and has been described in association with gastroesophageal reflux, exercise and psychological disorders. This case also underscores the need for flexible bronchoscopy for stridor since the diagnosis would have been missed with rigid bronchoscopy.

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THE EPIGENETICS OF NEONATAL NEUROPROTECTION

T. Cossey¹, M. Clarke¹, B. Sims^{1,2} ¹UAB, Birmingham, AL and ²UAB, Birmingham, AL.

Purpose of Study: Our study was designed to determine the role of specific epigenetic processes in neonatal neuroprotection. Neonatal brain injury is a devastating condition that represents a significant cause of neonatal morbidity and mortality. Retinoic acid (RA), a metabolite of vitamin A, has been shown to protect against ischemic brain injury in the mouse by mechanisms that are unclear. One potential protective pathway may involve epigenetic mechanisms such as histone deacetylase inhibition.

Methods Used: All animal procedures are approved by IACUC. Postnatal day 7 mice will be anesthetized using 3% isoflurane to induce anesthesia and 1.5% for maintenance. A mid-tracheal incision will be placed and the left common carotid exposed. The incision is approximated and surgical glue is used. Animals are allowed to return to normal then placed back with mother after site cleaned. Prior to induction animals will be treated with ATRA or mineral oil. After 24 hours, brains will be collected. Animals will be sacrificed by approved IACUC methods then brains will be placed in 4% paraformaldehyde for 12 hour then placed in 30% sucrose for 12-16hr. After brains embedded with sucrose, 12 micrometers sections will be collected using a standard cryostat.

For in vitro studies, neural stem cells were used. Cells were placed in high glucose-DMEM/N2 supplements and allowed to grow for 7 days prior to ATRA administration. After experimental conditions (3mM glutamate) for 24 hours, cells will plated on poly laminin-coated coverslips for 24 hours then

visualized using standard immunocytochemistry. All ATRA will be 100nM based on a dose response curve established in the Sims' laboratory. Cleaved caspase-3 was used to detect cell death.

Summary of Results: In our hypoxia-ischemia model, HDAC1 showed a dramatic increase in expression (78-fold) and is reduced significantly in the presence of RA. In the in vitro study, HDAC1 expression was not changed during excitotoxic stress. HDAC2 increased by about 29% in the glutamate-treated cells, and decreased back to control levels in the samples treated with glutamate and RA.

Conclusions: HDAC1 increases in the hypoxia-ischemia model and decreases in the presence of RA. HDAC2 expression is altered by RA treatment. Further studies are needed to examine specific HDAC isoforms in neonatal brain injury and the role of RA.

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HYPOTONIA AS THE FIRST SIGN OF TRANSIENT NEONATAL MYASTHENIA GRAVIS

M. Cuevas, RM. Whitehurst *USA Children's and Women's Hospital, Mobile, AL.*

Case Report: A male infant was born at 25 weeks, with a birth weight of 700 grams. The infant required intubation secondary to no respiratory effort and received surfactant; Apgars were 2-4-4. The initial gas in the first hour of life was pH 7.21, HCO₃ of 16 mmol/L, BE - 11. The infant continued to exhibit no respiratory effort and persistent hypotonia for the following 4 days of life and developed worsening anasarca. Imaging showed a gasless abdomen and a cranial ultrasound was within normal limits.

Prenatal history was remarkable for a 35 year old mother, G2 P1 with history of DM type 1 and hypothyroidism. She presented with fever and emesis, and was admitted for glucose control and hydration. She developed cardiopulmonary failure requiring CPR and recovered in 4 minutes. She was placed on a pancuronium drip to better control her ventilatory support. Due to the critical condition of the mother a Cesarean section was performed so as not to further compromise the infant. The mother deteriorated further and expired 5 days after delivery. Up to the time of death the mother never regained spontaneous respirations even after discontinuation of the pancuronium drip.

In light of the maternal history and, the persistent hypotonia of the child, Transient Neonatal Myasthenia Gravis was suspected and confirmed by acetylcholine antibody studies drawn on the mother. The results showed that acetylcholine blocking antibody was 26% (0-15), the acetylcholine binding antibody was negative and the acetylcholine modulating antibody was 5 % (0-20), which is consistent with the diagnosis of myasthenia gravis.

Transient Neonatal Myasthenia Gravis should be included in the differential diagnosis of a newborn with persistent hypotonia despite the lack of maternal history of myasthenia gravis.

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DETERMINATION OF ETHANOL METABOLITES IN PREGNANT, ABSTAINING, DIABETIC FEMALES: A PILOT STUDY

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Purpose of Study: Detectable levels of ethanol metabolites have appeared in the meconium of infants of abstinent diabetic mothers. One possible explanation for this finding is the fermentation of urinary glucose by bladder yeast (the "auto-brewery" phenomenon). This study seeks to clarify this process by examination of the urine of abstinent diabetic women for non-oxidative metabolites of ethanol.

Methods Used: Urine samples of 44 abstinent pregnant women (14 with gestational diabetes mellitus with fasting hyperglycemia, 15 with pregestational diabetes mellitus, and 15 non-diabetic controls) were analyzed via liquid chromatography and tandem mass spectrometry for the presence and amount of ethyl sulfate and ethyl glucuronide.

Summary of Results: Detectable levels of these ethanol metabolites were noted in 0% of women with gestational diabetes with fasting hyperglycemia, 6.7% of women with pregestational diabetes, and 13.3% of non-diabetic controls. None of the women had levels high enough to be considered positive.

Conclusions: The low-undetectable levels of non-oxidative ethanol metabolites in the urine of abstinent, pregnant diabetic women suggest that

the "auto-brewery" phenomenon most likely does not contribute to any significant ethanol production in these women. Other measures and methods may be needed to demonstrate if this process can explain the presence of ethanol metabolites in the meconium of the infants of some of these women.

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LEAD IN BLOOD TRANSFUSIONS IN EXTREMELY LOW BIRTH WEIGHT INFANTS

MT. ElAbiad, RE. Hook *University of Tennessee Health Science Center, Memphis, TN.*

Purpose of Study: Fetal lead (Pb) neurotoxicity is common with high maternal body Pb burdens at all stages of pregnancy. Premature infants have the same risk if co-transfused with packed red blood cells (PRBC) collected from unscreened donors.

Objective: to calculate the incidence of PRBC co-transfusion with a toxic Pb load in extremely low birth weight infants (ELBW) in the first week of life and with any given transfusion.

Methods Used: Infants with birth weights ≤ 1000 g were recruited and followed prospectively. Blood from the transfusion PRBC units was tested for Pb levels. The WHO has set a permitted weekly enteral intake of 25 mcg/kg. The intravenous equivalent was calculated as follows: 1) Bioavailability of Pb is 50% in children. 2) Urinary excretion via glomerular filtration accounts for 76% of daily Pb losses. The gastrointestinal secretions accounts for 16%. 3) The glomerular filtration rate in ELBW infants at the end of the first week of life is estimated to be 1/6 that of an adult. 4) With an extremely prolonged intestinal transit time in ELBW in the first week of life and a high intestinal reabsorption rate, the intestinal losses were estimated as insignificant. Thus a permitted weekly load of Pb intake was calculated as $25 \times 50\% \times 1/6 = 2.08$ mcg/kg. A daily permitted dose was also extrapolated.

Summary of Results: Over a 6 month period, October 2008-March 2009, 37 infants, birth weight 736 ± 157 , gestational age $25.7 \text{ weeks} \pm 1.7$, received ≥ 1 PRBC transfusions. A total of 325 transfusions were given, 36% in the first week of life. There were 2 infants (5.4%) that were co-transfused with a weekly Pb load considered toxic by WHO standards. There were 62 (19%) blood transfusion procedures that co-transfused 27 different infants (73%) with a toxic Pb load. 20 of 62 transfusions were ≥ 15 ml/kg orders. Only 11 of the 20 would still have given a toxic load if 10 ml/kg was ordered, a reduction by 18% on the original 62 transfusions.

Conclusions: PRBC Co-transfusion with a toxic load of Pb in ELBW infants is not uncommon with unknown long term neurotoxic consequences. This is the first study to show toxic Pb exposure from blood transfusions in this age group. There is a need to further evaluate this toxic exposure incidence and develop ways of prevention. For now, transfusion orders with 10ml/kg instead of 15ml/kg may be warranted.

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NEONATE WITH HETEROTAXY SYNDROME

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Case Report: Introduction: Heterotaxy Syndrome is a defect of laterality with abnormalities of the spleen, visceral malposition and maldevelopment. There are two types: Asplenia type or Ivemark syndrome (bilateral right-sidedness) and Polysplenia (bilateral left-sidedness) of which 89% total have malrotation of the intestines, 75% of which develop a volvulus.

Case Presentation: A 36 6/7 wk AGA Preterm male delivered via induced vaginal delivery to a 39 yr G4P2 Hispanic female with no history of alcohol, tobacco, or drug use. Pregnancy complications included pregnancy induced hypertension and Type 2 diabetes. Prenatal US showed fetal intraatrial defect and dextrogastric and a prenatal MRI showed no diaphragmatic hernia. Upon admission to the NICU a chest radiograph showed a midline liver, right-sided gastric bubble, and enlarged cardiac silhouette. Echocardiogram revealed a common atrium and absence of renal to hepatic inferior vena cava with azygous continuation. Abdominal ultrasound showed situs inversus and no spleen tissue seen. Subsequently enteral feedings were stopped for the presumptive diagnosis of asplenia heterotaxy syndrome. Upper GI with small bowel follow-through showed findings compatible with situs inversus, malrotation of the small bowel, and non-rotation of the large bowel with cecum in the left lower quadrant without volvulus. Pediatric Surgery team was consulted and suggested enteral feedings could be started due to no volvulus but the feedings were not tolerated. At the time of the consequent LADD procedure, multiple small spleens were seen. Diagnosis was changed

from asplenic to polysplenic heterotaxy syndrome, which also was more compatible with the less severe cardiac findings.

Discussion: Heterotaxy syndrome, while rare (4 in 1,000,000 live births), will commonly have malrotation and volvulus present, whether it is the asplenic or Polysplenic type. This case illustrates that when dextrogastria is present, malrotation and volvulus should be suspected, feeds withheld, and an evaluation for malrotation and volvulus should be done.

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BACILLUS CEREUS MENINGO-ENCEPHALITIS WITH DIABETES INSIPIDUS IN A PRETERM INFANT

MN. Hasan, M. Pourcyrus, AJ. Talati *University of Tennessee Health Science Center, Memphis, TN.*

Case Report: *Bacillus cereus*, a gram-positive, aerobic spore forming rod, is ubiquitous. Isolation of *Bacillus cereus* from a normally sterile site (i.e. blood, CSF) is often disregarded by clinicians as a specimen contamination. Very few cases of *Bacillus* meningitis are reported in preterm infants without any other risk factors. ELBW infants are very susceptible to infections secondary to poor immune status and develop severe infections like meningitis, brain abscess and rarely complications like central diabetes insipidus (CDI).

We report a case of 32-week SGA twin preterm infant with BW of 839 gm, delivered by c-section with no known risk factors. Initial course was uneventful except for mild respiratory distress requiring nasal CPAP. Infant was started on feeds with expressed breast milk with intermittent abdominal distension, but on the 10th day, she developed lethargy with worse abdominal distension requiring NPO status, antibiotics and later mechanical ventilation. She was transferred to our facility for further care. She developed seizures subsequently which responded to Phenobarbital. *Bacillus* species sensitive to Vancomycin was isolated from the initial blood. Spinal tap done later revealed evidence of meningitis (CSF glucose <6mg/dl, WBC 5500, 93% neutrophils) with negative culture. CRP peaked 33 mg/dl. Infant subsequently developed hypernatremia requiring fluid intake up to 200 cc/kg/day. CDI was diagnosed on clinical and biochemical parameters. Infant responded well to DDAVP with normal serum sodium levels. Head ultrasound, CT and MRI showed multiple cystic lesions and its drainage revealed purulent fluid. The patient received 6 wks of antibiotics, which included vancomycin, cefotaxime and meropenem. The infant was discharged home with Phenobarbital and g-tube feeding secondary to poor neurologic status.

Nonanthrax *Bacillus* species meningitis is rare. There have been very few reports of meningitis and brain abscesses with these bacteria in low risk preterm infants. Our case was unique with the development of CDI following *Bacillus* meningoencephalitis and brain abscess. It draws attention to the severe morbidity caused by a relatively benign and usually ignored organism. Prompt identification and treatment of this bacterial infection is warranted.

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MERCURY IN BLOOD TRANSFUSIONS IN EXTREMELY LOW BIRTH WEIGHT INFANTS

RE. Hook, MT. ElAbiad *University of Tennessee Health Science Center, Memphis, TN.*

Purpose of Study: **Background:** Mercury has been associated with fetal neurotoxicity as a consequence of antenatal exposure. This has been attributed to the high susceptibility of the developing fetal brain. Premature infants are also at a similar risk with packed red blood cells (PRBC) transfusions collected from unscreened donors as a potential exogenous source of mercury. Objective: to calculate the incidence of PRBC co-transfusion with a toxic mercury load in extremely low birth weight infants (ELBW).

Methods Used: Infants with birth weights ≤ 1000 g were recruited and followed prospectively. Data collected included infant's weight at the time of transfusion and the transfusion volume. Blood from the PRBC units used for the transfusion was tested for mercury levels. A load of transfused mercury was calculated per a given transfusion. This was compared to the allowed daily intake set by the US Environmental Protection Agency.

Summary of Results: Over a 6 month period, October 2008-March 2009, there were 37 infants, birth weight 736 ± 157 (mean $\pm$ SD), gestational age $25.7 \text{ weeks} \pm 1.7$ (mean $\pm$ SD) that received one or more PRBC transfusions. A total of 325 transfusions were administered during this period of which 77% were given in the first 28 days of life: 36% on 1st week, 19% on 2nd, and 11% on 3rd and 4th week. There were 22 (6.8%) blood transfusion procedures that co-transfused seventeen different infants (46%) with a toxic mercury

load. Five infants (14%) received 2 transfusions with a toxic mercury load. All 22 transfusions originated from 4 PRBC units. These gave 1, 4, 6, and 11 transfusions. Eight of 22 transfusions were ≥ 15 ml/kg orders. Only 3 of the 8 would still have given a toxic mercury load if 10 ml/kg was ordered, a reduction by 22% on the original 22 transfusions.

Conclusions: PRBC Co-transfusion with a toxic load of mercury in ELBW infants is not uncommon with unknown long term neurotoxic consequences. This is the first study to show the possibility of mercury exposure secondary to blood transfusions. There is a need to further evaluate the incidence of this toxic exposure and develop ways of prevention. In the mean time, transfusion orders with 10ml/kg instead of 15ml/kg may be warranted.

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GASTROSCHISIS TREATMENT AND OUTCOMES AT KOSAIR CHILDREN'S HOSPITAL: A TEN-YEAR REVIEW

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Purpose of Study: One of the first reported survivals of an infant with gastroschisis was published in England in 1878. Now, the incidence of gastroschisis is 0.94 per 10,000 live births worldwide. The 8-year incidence of gastroschisis in KY was 4.3/10,000 births (live and stillborn) from 1998–2005. This study is intended to be a descriptive analysis of the gastroschisis cases treated at Kosair Children's Hospital (KCH). Subsequently, we would like to address the feeding issues and postoperative complications these patients experience and ultimately compare their growth and development with other children their age.

Methods Used: Retrospective review of medical records of all patients with the diagnosis of gastroschisis from 1998–2007 who were cared for at Kosair Children's Hospital.

Summary of Results: A total of 110 infants with gastroschisis were treated at our institution from 1998–2007. There was a 95% survival rate. Mean gestational age was 35 weeks and the mean birth weight was approximately 2300 grams. The prevalence appears to be increasing and is known to be higher (four times baseline rate) when maternal age is less than 25 years old. The incidence is reportedly similar in male and female fetuses; but this study shows that two-thirds of the cases are male. Closure of the defect using a preformed silo has been associated with less morbidity. Postoperatively, prolonged dysmotility, which interferes with enteral feeding, is a common problem. Intestinal atresia and necrosis are associated with greater morbidity. Necrotizing enterocolitis is responsible for significant neonatal morbidity and has occurred in up to 10 percent of the cases. Long-term gastrointestinal problems related to bowel adhesions or short gut syndrome have also been seen, but are uncommon.

Conclusions: Due to limited information regarding the follow-up growth and development of patients with gastroschisis, more long-term information is needed. It would be interesting to see comparison growth of patients with gastroschisis to normal children at time of discharge, 6 months, 12 months, and 2 years. Is there catch-up growth? If so, when? With that information, neonatologist and pediatricians should join with surgeons and obstetricians to develop delivery and management guidelines in order to decrease morbidity and hospital stay.

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CHARACTERISTICS, MORTALITY, AND OUTCOME OF MASSIVE ANASARCA IN THE NEWBORN ICU

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Purpose of Study: Massive anasarca is an uncommon but severe condition in the NICU. A literature search failed to identify any studies of this problem. We therefore conducted a survey of massive anasarca over a two year period in a large NICU.

Methods Used: We reviewed computerized records (Neodata) for all admissions to our Regional NICU between 1/1/06 and 12/31/07. Infants whose weight rose $>30\%$ in a ten day period were included. We recorded demographics, daily weights, presumptive cause(s), and survival. The study was approved by the UAB IRB.

Summary of Results: Thirty seven (1.3%) of 2834 infants met criteria. 20 (54%) were male, 17 were white, 16 black, 2 hispanic and one was black/hispanic. The mean birthweight was 1256 grams with a range of 420–3920g, and mean gestation was 28 (23–39) weeks. The mean age at onset of anasarca was 32 (0–166) days and the mean time to maximum weight gain was

16 (0–66) days. The infants gained an average of 106% (37–315) from their weight at onset. Overall, 78% (29 of 37) of the infants died. Of those with renal failure, 86% (19 of 22) died, while 83% (19 of 23) with clinical or confirmed sepsis expired, and 75% (9 of 12) with NEC died. All 6 infants with congenital heart disease died. Many infants had more than one diagnosis.

Conclusions: Massive anasarca is uncommon but not rare. As our supportive abilities have improved, more infants are developing this devastating, highly lethal condition. Caring for these infants is extremely frustrating as there is no effective remedy for capillary leak. The systemic inflammatory response syndrome resulting from sepsis and/or NEC is a common cause of massive anasarca. Renal failure is common in these infants and further complicates management. Development of effective therapies for SIRS and capillary leak could significantly improve the outcome of these critically ill infants.

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ALTERED PHASE OF RESPIRATION WITH SWALLOW IN HEALTHY PREMIES AND INFANTS WITH BPD

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Purpose of Study: Swallow can occur at any phase of respiration (POR) during nonnutritive suck (NNS). This project will look at the relationship of swallow to POR during NNS.

Methods Used: Multi-channel graphs of NNS were collected with attention to swallow pressure, airflow, and chest motion. The low-risk preterm (LRP) infants were born at <35 weeks, no grade 3/4 IVH, no congenital anomalies and not likely to have BPD. 2 groups of infants likely to have BPD were randomized to receive or not receive a speech therapy treatment (BPDwithTX, BPDnoTX). Gestational age (GA), birth weight (BWT), gender, weeks before first nipple feed (WBFN), weeks since first nipple feed (WSFN), and number of swallows (SW) were compared against the POR incident to swallow [beginning expiration (BE), mid-expiration (ME), end expiration (EE), mid-inspiration (MI) or apnea (AP)].

Summary of Results: There were 176 swallows in the LRP group (35 studies, 16 infants). In the BPDnoTX group there were 135 swallows (31 studies, 15 infants). In the BPDwithTX group there were 76 swallows (20 studies, 11 infants). Significant relationships ($p < 0.05$) were noted in LRP infants (results given with OR). BE correlated with GA (1.4), WBFN (1.6) and WSFN (1.3). ME correlated with BWT (1.4) and WBFN (2.0). EE correlated with WSFN (0.7). MI correlated with SW (0.8). AP was negatively correlated with BWT (-0.3) and positively correlated with SW (1.2). Among the BPDwithTX group, BE correlated with BWT (0.2). In the BPDnoTX group, EE was associated with gender (0.3), BWT (1.2) and WBFN (1.4). There was a marginal association for EE with GA ($p = 0.0549$). AP was associated with GA (0.2), WBFN (0.3) and WSFN (0.8). When the BPD groups were combined, the only significant relationship remaining was for AP with WBFN (0.5).

Conclusions: There are predictable changes in the POR incident to swallow during NNS in LRP infants that are less clear in infants with BPD. This is consistent with other studies of infant feeding in which infants with BPD have dysmature development.

This work was supported by NIH Grant 5K23HD050581.

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CASE REPORT OF A HUMAN TAIL WITH SPINAL DYSRAPHISM

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Case Report: Purpose of Study: Human tail is a rare malformation associated with abnormalities of the spine and spinal cord. It is described as a finger-like appendage located in the lumbosacral region. A review by Lu et al. of 59 patients from 1960 to 1997 found that spinal dysraphism was the most frequently associated anomaly (49%), followed by tethered cord (20%) and lipoma (27%). Here we present a case which highlights the importance of advanced imaging for the diagnosis of underlying lesions.

Summary of Results: A 2 day old, term female was noted to have a finger like appendage arising just left of the lumbosacral spine at birth. Pregnancy

was notable for tobacco exposure and sacral anomaly on prenatal ultrasound. She was transferred to our hospital for further evaluation.

Admission physical exam was notable for 6 cm by 1cm soft tissue appendage projecting from the left buttock, about 2 cm left of midline, with slight narrowing at skin level. The remainder of the physical exam was normal. Spinal ultrasound showed abnormal extension of the spinal cord to the L5 level with large echogenic mass in the sacrococcygeal region. Spinal MRI demonstrated a lipomeningocele with tethered cord and possible hypoplasia of coccygeal segments. Outpatient surgical resection was planned by neurosurgery.

Conclusions: Human tail is a rare congenital anomaly that should alert the clinician of possible underlying spinal cord anomalies. A thorough neurological exam and detailed imaging is necessary due to the frequent association with spinal dysraphism and other anomalies.



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PATHOLOGICAL CONSEQUENCES OF VACUUM ASSISTED BIRTH

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Purpose of Study: Normal labor compresses the fetal head in both cephalic and breech presentations. Low segment placental implantation is compressed by the presenting part. Vacuum assisted delivery (VAD) of the fetal head reverses the force vectors of labor, pulling the head rather than pushing from behind; placement of the vacuum assist device may traumatize the edge or chorionic surface of the placenta.

Methods Used: We report three cases with adverse consequences, two with direct injuries to head and brain, and one indirect through traumatic laceration of fetal vessels on the placental surface, creating massive air embolism to the fetus.

Summary of Results: A male infant, BW 3370 g, 41 weeks, had severe direct traumatic injuries after four unsuccessful attempts at VAD, dying 136.5 hours after the ultimate spontaneous vaginal delivery. There was marked angulation of the medulla at the upper cervical spinal cord, herniation of the cerebellar tonsils into the foramen magnum, and sagittal oriented precystic necrosis and focal hemorrhage plus other intracranial effects. The second case was a 16 day old male infant, BW 3200 g, by vaginal delivery after three attempts of VAD. The infant collapsed suddenly at home; there was no evidence of overlay or suffocation. Subclinical incomplete fracture lines were found in the posterior skull, subtended by small old subdural hemorrhages. The thickened dura contained 2+ hemosiderosis. Attempted resuscitation included tibial intraosseous infusions with fat embolization to lung; the attempt elicited brief response but no sustained cardiopulmonary action. The third infant was delivered by section in the 38th week after induction by Cytotec(R) and four failed attempts by VAD. The fourth attempt resulted in abundant bleeding in part explained by a long laceration in the lower uterine segment. The male infant weighing 3500 g sustained a skull fracture and survived but with massive left hemispheric infarction in the downstream field of the left middle cerebral artery. Vector force analysis

demonstrated the particular result in the first case and traumatic laceration of placental vessels and intraplacental air emboli made likely air embolism as the principal cause of the intracranial lesion in the third case.

Conclusions: Vacuum assisted delivery may cause significant trauma to the fetal head or the placenta, with clinical significance.

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PANHYPOPITUITARISM ASSOCIATED WITH PERSISTENT PULMONARY HYPERTENSION: CASE REPORT

J. Surcouf, D. Felipe, A. Vargas, D. Rivera *Louisiana Health Sciences Center, New Orleans, LA.*

Case Report: A term male infant, birth weight 3kg, was born via repeat c-section. He had poor respiratory effort at delivery and received positive pressure ventilation. He was placed under an oxyhood and, at approximately 24 hours, had an acute desaturation event with subsequent need for intubation. A septic work-up was ordered and antibiotics were begun. CBC was unremarkable, but hypoglycemia was noted with blood glucose levels in the 20s. Dextrose infusions were initiated and he was transferred to a tertiary care hospital where an echocardiogram revealed persistent pulmonary hypertension (PPHN). He was begun on inhaled nitric oxide and 100% FiO₂. Over DOL 1, he required increasing ventilator support and developed pressor dependent hypotension. Despite increases in glucose infusion, episodes of hypoglycemia recurred. He was transferred to a regional medical center, where endocrinology was consulted due to persistent hypoglycemia, hypotension, and microphallus on physical exam. A work up for suspected hypopituitarism was initiated. With increasing ionotropic support and persistently labile ventilator settings, hydrocortisone supplementation was initiated on DOL 4. Clinical improvement was noted almost immediately. Glucose control was achieved, dopamine was discontinued by 48 hours and respiratory support weaned to extubation by DOL 9. ACTH-stimulation test performed prior to treatment confirmed cortisol deficiency. Additional laboratory results confirmed panhypopituitarism. The baby was discharged home on DOL 16 on growth and thyroid hormones and hydrocortisone therapy. Our presentation describes the association of pulmonary hypertension with hypoglycemia in the setting of hypopituitarism. In hypopituitarism, post-natal maladaptation will be ongoing, with continued lability of glucose and blood pressure control until deficient hormones are replaced. Standard treatment for PPHN was utilized in our patient, but true resolution of symptoms was not clearly evident until hydrocortisone supplementation was initiated. The association of congenital panhypopituitarism with PPHN has not been previously described.

Pulmonary and Critical Care Medicine Joint Poster Session

5:00 PM
Thursday, February 25, 2010

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PUMPLESS ARTERIOVENOUS CARBONDIOXIDE REMOVAL(AVCO2R): A NOVEL SIMPLIFIED STRATEGY FOR SEVERE ASTHMA

A. Aravantagi, K. Patra, S. Shekar, K. Scott *LSUHSC, Shreveport, LA.*

Case Report: Asthma is a common cause for admission to a pediatric intensive care unit and continues to have high mortality. ECMO has been used as the last resort in life-threatening asthma; however, it is a pumped circuit with severe complications like bleeding, hemolysis, fibrinolysis and tubing rupture. In contrast,arteriovenous carbon dioxide removal (AVCO2R) is a pumpless extracorporeal circuit which utilizes an arterio-venous pressure gradient to remove CO₂ and to add a small amount of oxygen via a gas exchanger. It has been shown to be highly effective in adults with acute respiratory failure.A 9 year old African American male with known history of moderate persistent asthma presented to the emergency room with status asthmaticus. He showed no improvement with inhaled beta agonists, inhaled anticholinergics,intravenous corticosteroids and intravenous magnesium. Non-invasive ventilation was not well tolerated and did not decrease his work of breathing; hence,he was intubated and transferred to our pediatric intensive care unit for respiratory failure. On arrival, he was on mechanical positive pressure ventilation with high peak pressures of 42 cm H₂O to deliver a tidal volume of 3cc/kg. The measured auto-positive end-expiratory pressure was 15 and the ventilatory flow waveform showed prolonged in-

complete exhalation.Arterial blood gas revealed severe respiratory acidosis with pH 7.09 and hypercapnia (pCO₂ 97).Different ventilatory modes to decrease the pressures and increase the minute volume were unsuccessful. In view of progressive hypercapnea and rapidly increasing pressures, we instituted an AVCO2R circuit with a 10F femoral arterial cannula and 16F venous catheter. The initial blood flow was 500 mL/min(20mL/kg/min).Within 3 hours of placement on AVCO2R, his pCO₂ decreased to 47 and pH improved to 7.23. The patient was on AVCO2R for a total of 7 days with improvement in lung compliance and gas exchange. He was extubated on day 10, transferred to pediatric floor on day 13, and discharged home in good condition on day 15. This case supports that AVCO2R is a less-invasive, cost-effective and is a promising technique as an alternate to ECMO in refractory status asthmaticus with hypercapnea.

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DEFINING IMPAIRMENT IN THE ELDERLY USING THE FORCED EXPIRATORY VOLUME IN 1 SECOND/FORCED VITAL CAPACITY RATIO

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Purpose of Study: To determine if a FEV₁/FVC less than 0.70, but above the lower limit of normal (LLN), correlates with clinically relevant functional status in an older cohort.

Methods Used: Subjects were recruited from the Louisiana Healthy Aging Study (LHAS) as a community-based sample. Pulmonary function tests were performed using Medgraphics PF Elite series equipment per ATS guidelines. Functional status was assessed using activities of daily living, quality of life, and respiratory symptoms questionnaires, as well as observer-assessed tests, which included a Six-minute walk test (6MWT) and the Continuous Scale Physical Functional Performance test (CS-PFP). Subjects were stratified into two groups per the FEV₁/FVC ratio being above 70% or between 70% and the lower limit of normal, as defined from population derived prediction algorithms. A group comparison was done by ANOVA statistical analysis to detect for differences in impairment. A statistical correlational analysis was then done to define the relationship between impairment and other pulmonary function variables: FEV₁, FVC, FEV₁/FVC, TLC, IC, DLCO, MIP, and MEP.

Summary of Results: A total of 97 subjects were tested. No statistically significant differences were detected between the two groups in any of the dependent measures of functional status. A medical history of wheezing and shortness of breath was found to be more prevalent in the group with an FEV₁/FVC between 70% and the LLN (p-values of 0.004 and 0.04, respectively). Exercise tolerance, as determined by 6MWT, was found to be diminished in this group, but did not reach statistical significance. The correlational analysis found that the relationship between functionality and pulmonary physiologic parameters was strongest for diffusing capacity and inspiratory capacity.

Conclusions: The decline in FEV₁/FVC with aging is poorly associated with functional status among healthy older adults. Alternative pulmonary function test parameters such as diffusing capacity and inspiratory capacity may be better indicators of functional status.

This work was supported by a grant from the National Institute on Aging (AG022064).

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MANAGEMENT OF SEVERE PULMONARY ARTERIAL HYPERTENSION IN A NEWBORN WITH PROXIMAL UREA CYCLE DISORDER

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Purpose of Study: Patients with Urea Cycle Disorders (UCD) commonly present with hyperammonemia, encephalopathy, seizures, and sepsis-like symptoms. Although reported, its presentation with Severe Pulmonary Arterial Hypertension (PAH) is less known. In this case report our aim is to help clinicians in promptly recognizing this presenting feature of UCD and to review the current management strategies, which would result in improved outcomes.

Methods Used: A Retrospective chart review and Medline and bibliographic search of relevant articles were performed.

Summary of Results: We report a term male infant who presented at 4 days of life with severe hyperammonemia ($>1200\mu\text{mol/L}$), shock, thrombocytopenia and respiratory failure. Initial workup showed low citrulline and high orotic acid levels consistent with proximal UCD. Patient underwent hemodialysis and was started on ammonul and buphenyl. An echocardiogram revealed severe PAH. Initial treatment of respiratory failure and PAH included conventional mechanical ventilation, inhaled Nitric Oxide (NO) 40ppm, 100% FiO₂, sildenafil, bosentan, surfactant, arginine and citrulline, and later neuromuscular blockade, inotropes, and high frequency oscillation. Patient's PAH gradually improved and he was discharged home on sildenafil, citrulline and buphenyl. At 5 month follow up patient's PAH was completely resolved and sildenafil was discontinued. He continues to be on citrulline and buphenyl as well as a low protein diet.

Literature review revealed that the pathogenesis of severe PAH in UCD is secondary to both quantitative and qualitative deficiencies of enzymes resulting in decreased levels of urea cycle intermediates including arginine, a precursor of nitric oxide. Genetic polymorphisms and mutations in enzymes have also been linked to altered metabolism of NO.

Conclusions: Our case demonstrates an uncommon but important clinical presentation of UCD. Low levels of Urea Cycle intermediates and NO are responsible for severe PAH. PAH as a presenting feature of UCD is probably both under-recognized and under-diagnosed. However, advances in the understanding of pathophysiology of UCD and PAH, improved availability of investigative therapies and continuing future research may help clinicians in better management of these patients.

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COMMUNITY-ASSOCIATED METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS PRESENTED WITH NECROTIZING PNEUMONIA AND SYSTEMIC THROMBOSIS

WM. Frandah, E. Martin, R. Raj, K. Nugent *TTUHSC, Lubbock, TX.*

Case Report: BACKGROUND: Necrotizing pneumonia due to community acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) has become increasingly common. CA-MRSA typically presents as an infection in the skin and the soft tissue, but can cause serious infection, including necrotizing pneumonia and septic shock. OBSERVATION: A 32 year old woman presented to the emergency room with shortness of breath, hemoptysis, right leg swelling, and diffuse muscle pain for 4 days. Noninvasive vascular lower extremity venous scan revealed a deep vein thrombosis in the right calf. Computed tomography of the chest with intravenous contrast did not show vascular filling defect but revealed multiple bilateral patchy infiltrates with the largest involving the left upper lobe, consistent with necrotizing pneumonia. The patient had a rapid and progressive course characterized by hypoxemia and persistent hypotension. Abdominal ultrasound was done and revealed thrombosis of the superior mesenteric, splenic, and main portal vein. Coagulation studies demonstrated that Protein C, S and Antithrombin III levels were all low. Blood and respiratory cultures grew methicillin-resistant *staphylococcus aureus*. Despite aggressive measures, the patient died 18 hours after presentation. DISCUSSION: Given its' increasing prevalence, rapid progression, and high mortality, a high level of suspicion should be maintained for CA-MRSA necrotizing pneumonia when a young, healthy, immunocompetent patient presents with hemoptysis and leukopenia. Certain staphylococcal virulence factors have been investigated, but to our knowledge, very little research documents a relationship between CA-MRSA necrotizing pneumonia and multiple systemic thrombi. This association may be the result of a specific staphylococcus virulence factor, an underlying hypercoagulable predisposition, or an undiagnosed pathology. Regardless of the cause, thromboses accentuated the severity of this case, and should be considered as a possible complication in future necrotizing pneumonia cases.

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A CASE OF CATCHING THE EMBOLI

J. Garcia, LS. Engel *LSU-Health Science Center, New Orleans, LA.*

Case Report: A 90-year-old woman with history of congestive heart failure, hypertension, atrial fibrillation, dyslipidemia, chronic obstructive pulmonary disease, cerebrovascular accident, and peripheral vascular disease presented to the emergency department (ED) with 3 days of visual hallucinations and altered mental status. During the initial evaluation in the ED, the patient was

disoriented, complained of having headaches, and carried on conversations with people who were not present. Vital signs at admission were; heart rate 64, blood pressure 198/88, temperature 98.6 oF, and respiratory rate 18 with oxygen saturation 98% on room air. Physical exam did not reveal any pulmonary, cardiovascular, or neurological abnormalities. A Folstein mini mental status exam was abnormally low with a score of 15. Arterial blood gas showed a respiratory acidosis on 3 L of oxygen. Urine analysis, urine cultures, blood cultures all were negative. Cat scan of her head did not reveal any ischemia, hemorrhage, or mass. CT angiogram of the chest was incidentally ordered and demonstrated a large obstructing saddle embolus of the right pulmonary artery. A transthoracic echocardiogram, obtained on day 2 of admission, showed left ventricular systolic dysfunction with an ejection fraction of 40–45%, inferior wall hypokinesis, moderate pulmonary hypertension, mild dilation of right atrium and right ventricle. The patient was started on full dose enoxaparin and warfarin for anticoagulation of the saddle embolus. The patient's altered mental status dramatically improved, returning to her baseline after 3 days.

Acute pulmonary embolism is a serious life threatening problem which can lead to high mortality if not diagnosed accurately. Classically, patients with massive pulmonary emboli present with hypotension, elevated central venous pressure, right ventricular failure, and hypoxia. However, the patient presented in this case never displayed any of the common symptoms or signs of respiratory distress, tachycardia, chest pain, or hypotension. This case demonstrates the difficulty of diagnosing pulmonary embolism due to the variability of presenting clinical symptoms.

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IMPACT OF RECOMBINANT HUMAN ACTIVATED PROTEIN C IN TREATMENT OF SEPTIC SHOCK IN A COMMUNITY HOSPITAL: IMPACT STUDY

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Purpose of Study: In controlled trials with strict protocols, treatment of severe sepsis with Recombinant Human Activated Protein C (RhAPC) has been shown to reduce mortality. However, in "real-life" these criteria may not be applied. Our objective was to study the characteristics and outcomes of patients treated with RhAPC in clinical practice in a community hospital.

Methods Used: We conducted a retrospective analysis of 36 cases who had received RhAPC for severe sepsis/septic shock in a 2-year period. Data included demographics, clinical variables and calculated Apache II score.

Summary of Results: Mean age of patients was 54.78 ± 14.78 , mean Apache II score was 24.11 ± 6.44 of which 75% survived (mean Apache II 23.7 ± 7.2) and 25% deceased (mean Apache II 25.3 ± 3.0). 23 patients received $\geq 50\%$ RhAPC dose (20 survived and 3 deceased) and 13 patients received 0–49% RhAPC dose (7 survived and 6 deceased, $p=0.08$). 25 patients received drug in <24 hours (17 survived and 8 deceased). 11 patients received drug in >24 h (10 survived with 1 death, $p=0.28$). Of 18 patients with Apache II <25 , 14 survived and 4 deceased; 18 patients with Apache II ≥ 25 , 13 survived and 5 deceased ($p=0.70$). 20 patients were blood culture positive (16 survived, 4 deceased), 16 were culture negative (11 survived, 5 deceased). 7 patients had ≤ 2 organ dysfunction (6 survived, 1 deceased), 29 patients had >2 organ dysfunction (21 survived and 8 deceased, $p=0.46$). 3 patients with no comorbidities prior to diagnosis of sepsis had 100% survival; Of 9 with single comorbidity 8 survived and 1 deceased; Of 24 patients with multiple comorbidities 16 survived and 8 deceased ($p=0.24$). Out of 36 patients only 1 had serious bleeding event.

Conclusions: RhAPC was beneficial in treatment of sepsis. The Survival advantage was more apparent in patients who received more than 50% of the target dose. Culture positive patients appeared to have better survival. Higher number of comorbidities and organ dysfunctions carried higher risk of mortality.

CLINICAL IMPLICATIONS: RhAPC when given before or after 24 hours appeared to be beneficial in severe sepsis.

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RARE CASE OF A MEDIASTINAL PLEOMORPHIC SARCOMA IN AN IMMUNODEFICIENT PATIENT

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Case Report: Pleomorphic sarcoma (widely known as malignant fibrous histiocytoma, or MFH) is a soft tissue sarcoma usually originating from the deep musculature of the extremities, retroperitoneum and trunk. The occurrence of this malignancy in the mediastinum is exceptionally rare. To our knowledge, only thirteen cases of MFH of the mediastinum have been previously reported. Furthermore, only three cases of MFH in patients infected with Human Immunodeficiency Virus (HIV) have been described in the literature, none of which occurred in the mediastinum (two were cutaneous and one in the small intestine).

A 44-year-old African American male without any significant past medical history complained of a two month evolution of epigastric pain radiating to the right chest. He denied weight loss, fever, night sweats, cough or nausea. On admission a chest radiograph revealed an enlarged mediastinum, followed by chest computerized tomography (CT) which identified a large mass in the posterior mediastinum. A percutaneous CT-guided biopsy was done which revealed a high-grade MFH. Staging did not reveal metastasis. He was also incidentally diagnosed with HIV with a CD4+ T-lymphocyte count of 641 cells/ μ L. The case was discussed with a multi-disciplinary team, and the consensus was that the patient should receive neoadjuvant radiotherapy, followed by restaging scans to determine potential resectability of the mass. Chemotherapy was deferred, unless the tumor grew despite radiotherapy, or if metastasis developed. Antiretroviral therapy was under consideration given presence of malignancy.

The rarity of this malignancy and uncommon site of presentation in association with an immunodeficient state makes this case unique. This is the first report in the literature of an HIV-infected patient presenting with this uncommon tumor in the mediastinum. The association between HIV infection and pleomorphic sarcomas may be coincidental considering the prevalences of both diseases. Whether or not immunodeficiency might be related to sarcoma development, or if concomitant treatment of both conditions improves overall survival (as seen in AIDS-related malignancies) remains to be determined.

236 NOVEL H1N1 INFLUENZA A VIRUS INFECTION IN A RENAL TRANSPLANT PATIENT PRESENTING WITH ABDOMINAL PAIN AND SEPTIC SHOCK

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Case Report: Novel H1N1 influenza A infections are being seen with increasing frequency as the epidemic progresses. Immunocompromised patients with the novel H1N1 influenza may have atypical clinical presentations.

A 45 year old man 3 years post kidney transplant presented with 7 days of fever, abdominal pain and vomiting. Contact history revealed his son's recent febrile respiratory illness and reported exposure to H1N1 positive classmates. The patient was febrile, tachycardic, hypotensive, hypoxic and tachypneic. Abdominal examination revealed diffuse tenderness and decreased bowel sounds; the pulmonary examination was unremarkable. Initial laboratory examination found leukocytosis (13.9 k/dl), hyponatremia (123 mmol/L), hyperkalemia (5.8 mmol/L), metabolic acidosis (HCO₃ 3 mmol/L, anion gap 40 meq/L), renal failure (BUN 157 mg/dl, creatinine 19.8 mg/dl), elevated CK (1118 IU/L), lipase (495 IU/L) and amylase (495 IU/L). CT of the abdomen and pelvis were unremarkable. Chest Xray was unremarkable; CT chest showed mild patchy peripheral opacities. BAL and pan-cultures were done on admission. Empiric therapy with oseltamivir, broad spectrum antibiotics, and supportive therapy with vasopressors, volume expansion, and ventilatory support was immediately begun. Continuous renal replacement therapy with citrate anticoagulation was initiated. Steroid support was provided; mycophenolate was discontinued. The patient eventually recovered in 2 weeks. Respiratory viral culture diagnosed influenza, later confirmed to be the novel H1N1 variety by PCR, despite an initial negative influenza screen. A detailed search found no bacterial, mycobacterial, fungal or other viral infection.

Review of literature shows that critically ill patients with novel H1N1 influenza infection may present with diarrhea (25%), vomiting (25%), and hypotension unresponsive to IV fluids (50%); what proportion of patients may present with predominant abdominal symptoms and no respiratory symptoms has not yet been established. Novel H1N1 influenza virus infection may mimic an acute abdominal infection with septic shock. Good contact history, a high index of suspicion, and definitive viral testing are necessary to appropriately diagnose and treat these patients.

A RASH AND SPONTANEOUS PNEUMOMEDIASTINUM

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Case Report: Spontaneous pneumomediastinum (SPM) is free air within the mediastinum without known precipitating cause. Usually this condition follows a benign course. However, there are instances where it may provide prognostic information and prompt further investigation for underlying lung disease.

A 54 year old woman presented with sore throat and rash on her face and shoulders. She was treated with antibiotics and steroids for pharyngitis. Her pharyngitis resolved but the rash persisted, and during a follow-up visit she was found to have elevated liver enzymes and CPK. After completing a course of steroids she presented to the emergency department with shortness of breath and cough. A chest CT revealed peripheral ground glass opacities and bronchoscopy with BAL was performed. Viral panel and cultures were negative, and the predominant cells in the BAL were monocytes/macrophages. Seromarkers for connective tissue disease, including anti-Jo-1, were negative. The patient was discharged home with mild clinical improvement on antibiotics and steroid taper. She was re-admitted two days later with progressive dyspnea, hypoxemia and evidence of pneumomediastinum which progressed to bilateral pneumothoraces. Her gas exchange deteriorated requiring mechanical ventilation. Repeat chest CT demonstrated diffuse bilateral ground glass opacities and she underwent lung biopsy, which revealed acute and organizing diffuse alveolar damage. Our clinical diagnosis was polymyositis/dermatomyositis (PM/DM) with acute interstitial pneumonia (AIP). Her respiratory failure progressed despite cyclophosphamide therapy and high dose steroids, and she died 10 weeks after her initial presentation.

Pneumomediastinum is caused by alveolar hyperinflation leading to rupture, with dissection along bronchovascular bundles into the mediastinum and the subcutaneous tissues. In a recent series, SPM was associated with underlying connective tissue disease in ~5% of consecutive cases. In a report of patients with PM/DM-associated lung disease, all 5 patients with AIP developed pneumomediastinum and all died. In patients with PM/DM-associated lung disease, SPM may be associated with increased mortality.

In patients with PM/DM, SPM should increase clinical suspicion for important underlying lung disease, including AIP.

238 PULMONARY HYPERTENSION IN SICKLE CELL DISEASE: IS IT ASSOCIATED WITH VASO-OCCLUSIVE CRISIS?

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Purpose of Study: Incidence of pulmonary hypertension (PHTN) in adult patients with sickle cell disease (SCD) ranges from 30–40%. In SCD patients PHTN increases the risk of early death with an estimated 2 year mortality rate close to 50%. The deformed red blood cells during the SCD crisis cause occlusion of microcirculation and end organ ischemia clinically manifesting as pain crisis. In the lung this has been proposed as the cause of PHTN. Based on this we decided to investigate the correlation between pain crisis and pulmonary hypertension. To investigate it we proposed the null hypothesis that average number of vaso-occlusive crisis for sickle cell patients with and without pulmonary hypertension is similar.

Methods Used: After IRB approval we did a retrospective chart review of 307 SCD patients followed in the sickle cell clinic at our Institute. Data was obtained on history, laboratory work and transthoracic echocardiography (ECHO). PHTN was defined as a RVSP > 35 mmHg on transthoracic echocardiography. Out of 307 patients 88 patients had ECHO data available.

Summary of Results: Out of 88 patients with ECHO data 62 had normal right heart function without PHTN and 26 patients (30%) were noted to have PHTN. The Wilcoxon Rank-Sum test was used to compare the two groups. Patients with sickle cell disease without echocardiographic evidence of pulmonary hypertension (N1 = 62) had sum of ranks for the sample (R1) of 2818.5 with a median of 48. Patients with sickle cell disease with pulmonary hypertension (N2 = 26) had R2 of 1097.5 with a median of 42.5 with a $|Z| < 1.987$. Thus the null hypothesis was accepted.

Conclusions: Our study showed no correlation between the number of vaso-occlusive crisis and presence of pulmonary hypertension in patients with SCD. In our SCD patient study group with available ECHO data, PHTN was seen in almost 1/3rd of the patients. Thus in view of the high incidence of

pulmonary hypertension in SCD patients and associated high mortality, the physicians should have a low threshold to screen for pulmonary hypertension.

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A LUNG NODULE, PLASMA CELLS AND LUPUS

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Case Report: A predominance of plasma cells is rarely found on lung biopsy and has been reported in both non-malignant and malignant conditions including granuloma, inflammatory pseudotumor, plasmacytoma, and lymphoma.

A 57 year old male was referred for evaluation of an irregularly shaped 2.5 × 3.0 cm right upper lobe nodule. He had been diagnosed recently with systemic lupus erythematosus (SLE) complicated by arthritis, antiphospholipid antibodies and nephritis. He had a 20 pack-year smoking history but quit 25 years earlier. A transthoracic lung biopsy was non-diagnostic, and showed a predominance of plasma cells. The nodule remained stable on serial CT scans for 2 years, after which surveillance was stopped. After 9 years of well-controlled SLE on hydroxychloroquine, the patient presented to rheumatology clinic with a cough and 10 pound weight loss over 3 months. Chest x-ray revealed bilateral pulmonary nodules, and chest CT scan demonstrated multiple pulmonary opacities with ill-defined borders and air bronchograms. No significant mediastinal adenopathy was seen. Fiberoptic bronchoscopy with transbronchial biopsies yielded fragments suspicious for lymphoma, but larger samples were requested by the pathologist. Open lung biopsy demonstrated a low-grade B-cell lymphoma most consistent lymphoplasmacytic lymphoma.

Lymphoplasmacytic lymphoma is a rare and relatively indolent malignancy which uncommonly affects the lungs. Parenchymal lung involvement by lymphoma can present as reticular interstitial disease, a solitary pneumonic infiltrate, or as multiple pulmonary masses with air bronchograms as seen in this patient. Existing literature supports an association between lymphoproliferative disorders (including lymphoplasmacytic lymphoma) and SLE, but whether one condition is causative for the other is unknown. To our knowledge this is the first report of pulmonary lymphoplasmacytic lymphoma associated with SLE. The plasma cells seen on the initial lung nodule biopsy are likely to have been an early manifestation of the low-grade lymphoplasmacytic lymphoma that became symptomatic nearly a decade later.

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EFFECTS OF MILK EXPOSURE ON CYTOKINE LEVELS IN AN IN VIVO AND IN VITRO MODEL OF MILK ASPIRATION

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Purpose of Study: The role of milk aspiration in lung injury has not been studied extensively and remains controversial. Our laboratory recently described neutrophilic lung inflammation in a mouse model of milk aspiration. In the current study, we evaluated the cell and cell products involved in neutrophil recruitment into mouse lungs after exposure to milk.

Methods Used: In vivo studies: 3–4 week old mice received 2.5 µl/gm of 50% formula milk intranasally after light sedation. Control animals received normal saline in a similar manner. Bronchoalveolar fluid (BALF) samples were collected at 1, 2 and 7 days after aspiration. In vitro studies: RAW 264.7 cells and MLE-15 cells were exposed to 0.1% or 1% formula milk for 6 hours while controls were exposed to standard media alone. After 6 hours, cells were washed and incubated in media for an additional 24 hours. IL-6, MIP-2 and KC levels were measured in BALF and cell media using commercially available ELISA assays.

Summary of Results: In vivo: A significant increase in the level of IL-6 in the BALF at 24 hours and 48 hours was evident among mice exposed to milk (9.96 pg/ml, 4.18 pg/ml 24 and 48 hours after milk aspiration, versus 3.48 pg/ml for controls). There was also a significant increase in the level of KC in the BALF at 24 hours after milk exposure (361.62 pg/ml versus 17.53 pg/ml for controls). However, while there was an increase in MIP-2 levels in the BALF at 24 hours after milk exposure, the difference was not statistically significant. In vitro: A significant increase in the levels of MIP-2 and KC was seen in media from MLE-15 cells exposed to 1% milk (105.76 pg/ml versus

54.38 in controls for MIP-2; 1559 pg/ml versus 1521.8 pg/ml in control for KC). MIP-2 and KC levels were not increased in media from RAW 264.7 cells. Milk exposure did not induce IL-6 release from RAW 264.7 or MLE-15 cells.

Conclusions: Our study shows that exposure to milk results in an increase of proinflammatory cytokines in both in vitro and in vivo models, specifically those responsible for neutrophil chemotaxis. Further studies are needed to define the mechanism by which milk induces release of cytokines from lung cells.

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CD4+CD25+FOXP3+ TRANSFORMING GROWTH FACTOR-BETA-PRODUCING T CELLS ARE PRESENT IN MURINE TUBERCULOSIS AND ENHANCED IN ALCOHOL-CONSUMING MICE

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Purpose of Study: Regulatory CD4+CD25+Foxp3 TGF-beta-producing T cells in Mycobacterium tuberculosis infection are poorly described, but these cells may contribute to mycobacterial persistence. We evaluated TGF-beta+ lung CD4+CD25+Foxp3+ T cells in a murine TB model with mice on a liquid ethanol diet.

Methods Used: BALB/c mice were fed liquid alcohol or control diet then infected with 100 cfu M. tuberculosis H37Rv intratracheally. At 14, 21, and 28 days post-infection, single cell suspensions of lung cells were obtained and stained for surface marker expression (CD3, CD4, CD25) and intracellular Foxp3 and TGF-beta production (after in vitro stimulation with anti-CD3 and anti-CD28 and addition of brefeldin). Cells were then analyzed for surface markers and cytokines with a FACS Aria. Unstimulated cells and isotype monoclonal antibodies were used as controls.

Summary of Results: FACS analyses revealed TGF-beta-producing CD4+CD25+Foxp3+ T cells are present in the lungs of infected mice as shown in the table.

Conclusions: There are more CD4+CD25+Foxp3+TGF-beta+ T cells present in the M. tuberculosis infected lungs of mice on alcohol. TGF-beta-producing CD4+CD25+Foxp3+ regulatory lymphocytes may play a role in the persistence of mycobacteria in murine pulmonary TB.

	Fox+CD4+25+(%)		TGF-beta + CD4+25+ Fox+ (%)	
	Control	LED	Control	LED
Day 14	46.3	44.2	0	0.2
Day 21	40.7	36.3	2.8	4.4
Day 28	45.3	40	7.7	55

n=5/grp; data are mean±SEM

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CUFF LEAK TEST FOR THE DIAGNOSIS OF UPPER AIRWAY EDEMA

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Purpose of Study: Laryngeal edema occurs in up to 30% of patients on mechanical ventilator. Hoarseness of the voice has been used to assess the presence of laryngeal edema in patients with angioedema. We conducted a prospective study to evaluate the utility of the cuff leak test in assessing laryngeal edema comparing patients with normal voice to those with hoarseness and stridor post extubation.

Methods Used: Consecutive patients requiring mechanical ventilation between May 09 and October 09 in medical ICU were studied. Consent was obtained from the patients or their family members. Weaning parameters were obtained and a cuff leak assessment was performed. The inspired tidal volume was measured for 6 breaths with the cuff inflated. The expired tidal volume was measured for 6 breaths with the cuff deflated and the lowest 3 values were used. The patient was assessed for stridor and the voice quality was assessed between 30-60 min post extubation. Extubation failure was defined as re-intubation within 24 hours of extubation.

Summary of Results: Twenty four patients were included in the study after excluding patients from whom consent cannot be obtained. There were 16 males and 8 females, median age 56 years (18–84), median duration of

intubation 3 days (0–19). The overall median tidal volume used was 450ml (320–600) which was 6.4 ml/Kg ideal body weight (4.17–8.7). The median cuff leak was 195.3 ml (–32.6 – 455.8) which was 45.1 % (–7.6–99.27) of the tidal volume. Ten patients (41.6%) had hoarseness, 6 (25%) had a weak voice, 3 (12.5%) had stridor, and 5 (20.8%) had a normal voice. The median cuff leak % in the patients with normal voice was 48.7% (17.5–87.4), those with weak voice 51.5% (–7.65–76), and those with hoarseness had a cuff leak median of 14.9% (–6.2–93.2). The 3 patients with stridor had a cuff leak percent median 76.6 range from 44.8%–99.3%. There was one re-intubation for a patient with hoarseness.

Conclusions: The cuff leak test at the time of extubation can be used to assess for laryngeal edema. A cuff leak that was 15% of the inspired tidal volume suggests airway edema as evidenced by hoarseness of the voice. Cuff leak does not appear to predict stridor in this population. This preliminary data will be confirmed by enrolling more patients in the study.

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A CASE OF ACUTE METHEMOGLOBINEMIA SECONDARY TO USE OF 20% BENZOCAINE SPRAY FOR TEE

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Case Report: Benzocaine is a local anesthetic used as 20% topical spray for procedures like nasogastric tube insertion, intubation, and endoscopies. Benzocaine is known to produce varying degrees of Methemoglobinemia, an altered state of hemoglobin that impairs oxygen delivery to the tissues.

A 50-year-old man with history of intravenous drug abuse, hypertension, coronary artery disease, bacterial endocarditis, and embolic stroke underwent an elective trans-esophageal echocardiogram (TEE) to evaluate for vegetations. The patient received a two-second dose of benzocaine topical spray to his oropharynx a few minutes prior to the TEE. The patient tolerated the procedure well, however, immediately after the procedure he felt diaphoretic, confused and his oxygen saturations dropped to 80–85%. His skin color changed to a bluish discoloration. The patient was kept on nasal cannula, but his oxygen saturations did not improve. On further review, the patient denied any history of allergies or family history of inherited blood disorders. Physical exam was benign except for Mitral regurgitation murmur secondary to his endocarditis and skin discoloration. Methemoglobinemia was confirmed by arterial blood gas which revealed a methemoglobin level of 42.4% (Normal level 0–1%). The patient received one ampoule (50 mg) of intravenous methylene blue. The patient's symptoms resolved completely in one hour and his methemoglobin levels decreased to 7.1%, 1.1% and < 1% over the next 1, 3 and 5 hours, respectively.

Patients with methemoglobinemia usually present with cyanosis, anxiety, tachycardia, dyspnea, lightheadedness, confusion, and dizziness. The severity of symptoms correlates with the level of methemoglobin. Usually symptoms appear when the levels are above 10%. Diagnosis is suspected when cyanosis occurs in the face of a normal arterial PO₂ as obtained by ABG in patients. Methemoglobin level or saturation will confirm the diagnosis. Pulse oximetry is inaccurate in monitoring oxygen saturation in these patients. Management involves discontinuation of offending agent and administration of Methylene Blue. Symptoms resolve usually within 15–30 minutes.

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FATIGUE DURING INFANT CPR: ARE GUIDELINE CHANGES NEEDED?

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Purpose of Study: The AHA's 2005 CPR guidelines emphasized BLS skills by recommending to push hard and fast during chest compressions (CC). This may result in increased rescuer fatigue. Little is known about rescuer fatigue during two-thumb CC on infants. We hypothesize that rescuer fatigue will develop prior to the recommended two-minute change interval during two-thumb infant CC.

Methods Used: Fifty BLS/PALS certified health care providers were tested using a metronome set at 100 bpm and the Laerdal HeartCode BLS baby manikin connected to a computer and software. Compression depth (CD), rate, and chest recoil were recorded as measures of objective fatigue (OF). Subjects reported subjective fatigue (SF) as arm/hand discomfort or a desire to change rescuers due to feelings of inadequate performance. After a coach-

ing session, two scenarios were tested: Scenario 1 (S1): five minute cycle of continuous CC, and Scenario 2 (S2): five minutes of CC using a 15:2 compression ventilation ratio. An adequate CC was defined as >30 mm depth, reflecting 1/3 of the AP chest diameter, with adequate recoil as >90% (27mm). Subject variables included age, sex, height, weight, and glove size. Statistical analysis was done using ANCOVA and McNemar's test. A p-value of <0.05 was considered significant.

Summary of Results: There was no significant decrease in CD, rate or chest recoil during S1 as measures of OF. Mean CD during S1 demonstrated small incremental changes ending only one mm below the recommended depth of 1/3–1/2 the AP chest diameter. Conversely, the mean CD during S2 was acceptable throughout. SF developed at two minutes in 48% (24/50) of rescuers during S1 compared to only 22% (11/50) of rescuers during S2 (p value 0.002). Over five minutes, 82% described fatigue in S1 vs. 66% in S2 (p value 0.021). Average recoil was <27 mm throughout both scenarios.

Conclusions: Continuous CC results in significantly more rapid development of SF despite no development of OF. Our results suggest that the current interval for rescuer change during two-thumb CC is appropriate despite development of SF. Incomplete chest recoil was present throughout both scenarios suggesting that feedback devices are needed to monitor full chest recoil during infant CPR.

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DIFFUSE ALVEOLAR HEMORRHAGE IN A PATIENT WITH HEPATITIS C AND CRYOGLOBULINEMIA

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Case Report: Background: Alveolar hemorrhage is an unusual diagnosis rarely caused by cryoglobulinemia. Although this scenario is mentioned in case reports within the literature, it is a rare event and no standardized treatment exists.

Objective: To describe the case of a 58 year old male with HCV cryoglobulinemia and diffuse alveolar hemorrhage (DAH) and to review the literature available of this rare combination of diseases.

Case Report: This patient is a 58 year old male who was admitted for abdominal pain that was thought to be related to cholecystitis. This patient had chronic active HCV for 20+ years. During admission the patient developed purpura, azotemia, shortness of breath and hemoptysis. Cryoglobulins were abnormally high (0.417mg/mL). He was started on pulse steroids but the patient ultimately required intubation and mechanical ventilation for support. A bronchoalveolar lavage was performed and was consistent with DAH. Plasmapheresis was started, however there was no improvement in oxygen requirements. Patient eventually died and autopsy confirmed the clinical diagnosis of DAH.

Discussion: In each case report reviewed steroids were used with varying responses. The patient described by Gomez-Tello et.al, had a relapsing course of DAH that was refractory to steroids. It was speculated that either the virulence of the particular HCV genotype or the administration of steroids created an environment for viral replication and allowing for further immune complex deposition. They concluded that steroids could be more harmful than good in treating DAH. Although there has been some success in treating HCV related cryoglobulinemia and DAH with immunosuppressors, plasmapheresis, steroids, and cyclophosphamide, it is clear that there is no standardized treatment and therapy must be individualized for this rare and devastating complication.

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PULMONARY ALVEOLAR MICROLITHIASIS

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Case Report: Pulmonary Alveolar Microlithiasis (PAM) is a rare idiopathic disease with unknown etiology and pathogenesis. The diagnosis is usually made incidentally on radiological imaging. There are no definite treatments for this condition.

Summary: A 73 year old African American man with history of asbestos exposure and chronic obstructive pulmonary disease (COPD) diagnosed in 2000 and maintained on home oxygen since 2004 presented to the emergency department with increasing shortness of breath. Initial chest radiography showed extensive bilateral deposits with a "sand storm appearance". Subsequent computed tomography of the chest revealed that his lungs were filled

with multiple small calcifications and ground glass opacities with air bronchograms involving all lobes, consistent with diffuse alveolar microlithiasis. Arterial Blood Gas showed hypercapnic, hypoxemic respiratory failure. With these findings, the patient was placed on a 100% non-breather, aggressive pulmonary toilet and was started on treatment for presumed COPD exacerbation with nebulizers, antibiotics, steroids with placement in the intensive care unit for close monitoring. The patient was also placed on BiPAP due to his impending respiratory failure. During the hospital course, the patient began to show steady respiratory improvement with decreased oxygen requirement, weaned off BiPAP, and was switched to oral steroids and antibiotic. The patient was discharged home with home oxygen and pulmonary follow-up for his pulmonary alveolar microlithiasis.

PAM is a rare idiopathic condition that may have familial predisposition. PAM is usually asymptomatic for many years to decades and often diagnosed incidentally on radiological imaging. This disease is characterized by widespread intra-alveolar calcium deposits throughout the lung. It has a classic "sand-storm" appearance on chest radiography. There are no definite treatment options, and it carries a poor prognosis in its late stage. Since PAM is an indolent disease, earlier manifestations of this condition can be mistaken for other common entities of pulmonary disease such as COPD as with the case presented here.

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AMERICAN SOCIETY OF ANESTHESIOLOGISTS SCREENING QUESTIONNAIRE FOR OBSTRUCTIVE SLEEP APNEA: PERFORMANCE CHARACTERISTICS AND RECOMMENDED CHANGES TO IMPROVE SENSITIVITY, SPECIFICITY AND SIMPLICITY

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Purpose of Study: Screening methods for obstructive sleep apnea are cumbersome and unreliable. The ASA proposed a screening tool for OSA but the questionnaire is long and little data exist on its performance characteristics. This study was designed to determine the performance characteristics of the ASA questionnaire and to create a modified version that would improve its ease of administration, sensitivity and specificity.

Methods Used: The ASA screening questionnaire was prospectively administered to patients undergoing laboratory polysomnography. Data were collected on 100 consecutive patients and analyzed.

Summary of Results: The study population consisted of 40 male and 60 female patients aged 19 to 88 years (mean 52, SD 15) with BMIs of 23 to 63 (mean 36, SD 8). Patients underwent 86 diagnostic and 14 split night sleep studies and had an AHI of 0 to 147 (mean 22, SD 28). The screening tool comprises of a total of 3 sections and 13 questions. We found that out of the original 13 questions, retaining the 4 questions pertaining to BMI, snoring and sleepiness significantly shortens the questionnaire without sacrificing the sensitivity or specificity. Table 1 outlines ASA questionnaire performance characteristics of the 13 point ASA questionnaire and that of the shortened 4 point questionnaire.

Conclusions: The recommended simplified 4 point version is shorter, easier to administer, and has slightly better sensitivity and specificity. Simplification of the screening tool while maintaining the performance characteristics will make its adoption in clinical practice more likely.

TABLE 1

PARAMETER	SENSITIVITY	SPECIFICITY
ASA Questionnaire (overall) (OSA, AHI>5/hr)	91%	30%
ASA Questionnaire (overall) (OSA, AHI>15/hr)	88%	19%
ASA Questionnaire (Section A only) (OSA, AHI>5/hr)	66%	53%
ASA Questionnaire (Section A only) (OSA, AHI>15/hr)	72%	50%
ASA Questionnaire (section B only) (OSA, AHI>5/hr)	94%	28%
ASA Questionnaire (section B only) (OSA, AHI>15/hr)	95%	20%
ASA Questionnaire (section C only) (OSA, AHI>5/hr)	88%	21%
ASA Questionnaire (section C only) (OSA, AHI>15/hr)	84%	14%
Recommended simplified ASA Questionnaire (OSA, AHI>5/hr)	92%	30%
Recommended simplified ASA Questionnaire (OSA, AHI>15/hr)	95%	23%

Performance characteristics of individual components of the original ASA questionnaire and the simplified version.

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HYPERTHYROIDISM IS ASSOCIATED WITH REVERSIBLE PULMONARY HYPERTENSION

S. Vallabhajosula, S. Radhi, C. Cevik, K. Nugent *Texas Tech University Health Sciences Center, Lubbock, TX.*

Purpose of Study: Hyperthyroidism is an important but under recognized cause of pulmonary hypertension. We report a patient whose pulmonary hypertension responded well to the early recognition and management of her hyperthyroidism.

Methods Used: Case analysis and literature review.

Summary of Results: A 68-year-old Caucasian woman presented with exertional dyspnea and palpitations. She had no significant past medical history. Social history was positive for smoking and alcohol abuse. On examination she had mild diffuse thyromegaly. Her chest x-ray was normal. Pulmonary function tests did not reveal either obstructive or restrictive lung disease. Thyroid function tests revealed a TSH of <0.01mIU/L and a free T4 of 5.30ng/dl. Thyroid ultrasound showed a diffuse goiter with a solitary nodule in the right lobe. The radioactive iodine uptake scan of thyroid showed homogenous uptake. Her pro BNP was 1464. Echocardiography revealed a normal ejection fraction (60-64%), pulmonary artery systolic pressure (PASP) of 67-72 mmHg, right ventricular hypertrophy, mild dilation of the left and right atria, and mild tricuspid regurgitation. She was started on methimazole 20 mg twice daily and atenolol 25 mg twice daily. At a six month follow up she has no shortness of breath or palpitations. Repeat echocardiography showed a significant reduction of the PASP to 43-48 mmHg. Our review of the literature identified 8 studies with 77 patients who had pulmonary hypertension associated with hyperthyroidism. These patients had both Grave's disease and nodular goiter. The mean PASP was 47.5 mmHg. The response to medical or surgical therapy was excellent with post treatment pressure mean of 31 mmHg.

Conclusions: Patients with hyperthyroidism have endothelial dysfunction which leads to impaired production of vasodilators and increased expression of vasoconstrictors. Our case and our literature review demonstrate that patients with pulmonary hypertension and hyperthyroidism respond well to both medical and surgical management of their thyroid disease. All patients with pulmonary hypertension should have thyroid studies.

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BIPHASIC DEFIBRILLATION IN PEDIATRIC CARDIAC ARREST

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Purpose of Study: While all new commercially available defibrillators use biphasic waveforms, little is known about the efficacy of this newer technology in actual victims of pediatric cardiac arrest.

Methods Used: Single center, retrospective review of cardiac arrest records in a large quaternary care children's hospital. All shocks were delivered using rectilinear biphasic waveforms (Zoll Medical, Chelmsford, MA). Descriptive statistics were calculated using Microsoft Excel.

Summary of Results: 20 cardiac arrests were identified in 18 patients receiving biphasic defibrillation. 55% were male; median age was 2.5 years; median weight was 21 kg. Mean first shock dose was 2.6 J/kg, and mean second shock dose was 3.4J/kg. First, second, and third shock success was 4/20 (20%), 2/10 (20%), and 2/8 (25%) respectively. For events of less than five minutes duration, first shock success occurred in 3/11 patients (27%). 10/20 patients survived the resuscitation event.

Conclusions: Pediatric biphasic defibrillation success rates are much worse than those described in most adult studies. Short arrest duration was not associated with a high level of first shock success. Reasons for this discrepancy are unclear. Further analysis and study are needed to identify factors associated with failure of pediatric biphasic defibrillation in order to improve this essential treatment modality for pediatric cardiac arrest.

Renal, Electrolyte and Hypertension**Joint Poster Session**

5:00 PM

Thursday, February 25, 2010

250**TREATMENT OF OBSTRUCTIVE SLEEP APNEA WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) DOES NOT REDUCE ALDOSTERONE LEVELS IN HYPERTENSIVE PATIENTS**M. Acelajado, R. Pisoni, DA. Calhoun *University of Alabama at Birmingham, Birmingham, AL.*

Purpose of Study: Primary aldosteronism (PA) and obstructive sleep apnea (OSA) may be causally related in hypertensive patients. We hypothesized that OSA stimulates aldosterone release. If so, CPAP was predicted to reduce aldosterone levels in hypertensive patients.

Methods Used: Patients with hypertension and suspected OSA who were referred to the University of Alabama at Birmingham Sleep-Wake Disorders Center were prospectively evaluated with polysomnography, plasma aldosterone concentration (PAC), plasma renin activity (PRA) and 24 hour urine aldosterone (UAlto). Biochemical parameters were measured before the baseline sleep study and after 6 to 12 weeks of CPAP use.

Summary of Results: A total of 11 hypertensive patients on a stable anti-hypertensive drug regimen were evaluated. All patients had sleep apnea (mean apnea hypopnea index 13.52) and were prescribed CPAP (mean use 5.14 hours/night). Mean PRA, PAC and UAlto levels are summarized in the table. Nine patients were adherent to CPAP (mean use 5.84 hours/night). In evaluating adherent patients only, CPAP use raised plasma aldosterone levels significantly (mean change 2.711 ± 3.355). The effect on PRA and UAlto were not significant.

Conclusions: In patients with hypertension and OSA, CPAP use did not significantly change the levels of PAC, PRA or UAlto. Patients adherent to CPAP had a significantly higher PAC after at least 6 weeks of CPAP use. Overall these results do not support the hypothesis that untreated OSA stimulates aldosterone release.

	Pre-CPAP	Post-CPAP	P Value
PAC	10.39 ± 7.46	8.68 ± 7.53	0.162
PRA	9.19 ± 12.18	8.25 ± 9.96	0.624
UAlto	10.63 ± 9.11	9.76 ± 6.11	0.595

251**REDUCED DISTAL NEPHRON SODIUM REABSORPTION IN CYP1A1-REN2 TRANSGENIC RATS WITH INDUCIBLE ANG II-DEPENDENT MALIGNANT HYPERTENSION**Z. Alam, KD. Mitchell *Tulane University, New Orleans, LA.*

Purpose of Study: ANG II exerts a direct stimulatory action on distal nephron sodium reabsorption in normotensive states. However, the ANG II-dependence of distal nephron sodium reabsorption in ANG II-dependent forms of hypertension remains uncertain; in particular, in ANG II-dependent malignant hypertension. The present study was performed to determine the ANG II-dependence of distal nephron sodium reabsorption in Cyp1a1-Ren2 transgenic rats [strain name: TGR(Cyp1a1-Ren2)] with inducible ANG II-dependent malignant hypertension.

Methods Used: To assess distal nephron sodium reabsorptive function, we compared sodium excretion before and after blockade of the two main distal nephron sodium transporters, the amiloride-sensitive apical membrane sodium channel and the apical membrane sodium chloride cotransporter, by intravenous administration of amiloride (AMIL; 25 µg) plus bendroflumethiazide (BFTZ; 25 µg) in pentobarbital sodium-anesthetized male Cyp1a1-Ren2 transgenic rats (n=5).

Summary of Results: Cyp1a1-Ren2 transgenic rats induced with 0.3% I3C for 8-10 days exhibited a markedly elevated mean arterial pressure (MAP; 185 ± 5 vs. 131 ± 3 mmHg, $P < 0.001$) compared with non-induced rats (n=5). Administration of AMIL+BFTZ did not alter MAP in either group, but elicited a greater increase in urinary sodium excretion in the non-induced control rats than in the hypertensive rats (6.36 ± 1.08 vs. 3.13 ± 0.42 µEq/min, $P < 0.05$). Distal nephron sodium delivery was not different between the two groups (7.43 ± 1.41 vs. 5.24 ± 0.86 µEq/min). However, absolute distal nephron sodium reabsorption and fractional reabsorption of distal nephron sodium delivery were markedly lower in the hypertensive rats than in the

normotensive rats (3.13 ± 0.42 vs. 6.36 ± 1.08 µEq/min and 63.37 ± 7.86 vs. 87.97 ± 4.58 %, respectively, $P < 0.05$ in both cases).

Conclusions: These findings demonstrate that distal nephron sodium reabsorptive function is markedly decreased in Cyp1a1-Ren2 rats with ANG II-dependent malignant hypertension. Such impaired distal nephron sodium reabsorptive function suggests that ANG II-dependent stimulation of distal nephron sodium reabsorption does not contribute substantively to the hypertension in these rats.

252**NEW METHOD FOR PREDICTION OF ACUTE KIDNEY INJURY (AKI) IN CANCER PATIENTS BASED ON GRADIENT CHANGE WITH SERUM CREATININE(SCr)AS BIOMARKER**S. Alam^{1,2}, G. Nowshad¹, MH. Rahbar², A. Salahudeen¹ *MD Anderson CC (MDACC), Houston, TX and ²Center for Clinical and Translational Sciences (CCTS), Houston, TX.*

Purpose of Study: Dichotomy exists in AKI definition by AKIN and RIFLE with regard to cancer patients. Moreover, slow rate of SCr production in cancer patients makes it hard to predict AKI. To overcome this limitation, we redefined AKI based on gradient change for better sensitivity and specificity.

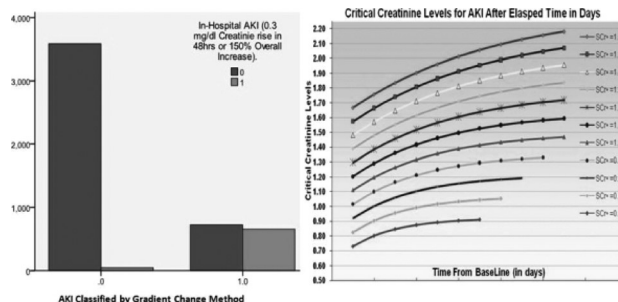
Methods Used: Multivariate, logistic, Multilevel and Mixed model analyses were performed by STATA 10MP. We developed new method to estimate AKI among cancer patients based on gradient change theory and established new equation with random intercept regression model (fig1).

Summary of Results: There were 51.3% men with mean(sd) age of $54.2(\pm 17.5)$ years. 71.9% were Caucasians, 9.3% Black, 13.6% Hispanic and 5% Asians. Incidence of AKI as per AKIN criterion is 14.2% during hospital stay. We performed comparison by kappa statistics and McNemar's test. The overall agreement is 84.6%. Also, this method correctly classified non-AKI conditions with probability 82.3%. (fig2) Considering AKIN criterion as Gold Standard, sensitivity and specificity of our new method remained 93% and 83% respectively. (fig3-4) Multivariate logistic regression analysis were performed with AKI as outcome variable based on new classification. The AKI was significantly associated with DM, BMT, ICU, PACU and length of hospital stay. (fig5)

Conclusions: Our AKI classification method is based on gradient change theory and has a stronger association with patient treatment effects and mortality; and early predicts the AKI patients who would otherwise remained undiagnosed.

$$Cr_{cr} = Cr_{bl}^{0.95} \left[\frac{3 - e^{-\left(\frac{t - t_0}{2} Cr_{bl}^{1.2}\right)}}{2} \right]$$

Cr_{cr} is critical creatinine level at time t days. Cr_{bl} is the baseline creatinine taken at previous time t_0 . Any creatinine levels above Cr_{cr} are predicted as AKI. Based on our new method, we established 27.5% in-hospital AKI incidence rate.

**253****MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS WITH MONOCLONAL IGG DEPOSITS**HM. Alshayeb^{1,2}, R. Canada¹, A. Alabsi¹, P. Walker³, L. Razavi¹, BM. Wall^{1,2} *¹UTMEM, Memphis, TN; ²VAMC, Memphis, TN and ³Nephropathology Associates, Little, AR.*

Case Report: Introduction: This report presents a patient with nephrotic syndrome due to membranoproliferative glomerulonephritis (MPGN) associated with glomerular monoclonal IgG kappa deposits, occurring in the absence of multiple myeloma (MM).

Case report: 39 yr old male with discoid lupus reported right sided pleuritic chest pain, cough, dyspnea, fever, and diffuse arthralgia. He denied voiding complaints or edema. He was afebrile, BP:143/80 mmHg, HR:87/min, and RR:22/min. He had hypopigmented skin lesions over the face and trunk. Breath sounds were decreased on the right chest with dullness to percussion. There was no edema.

Laboratory: WBC:6.3 K/mm³, Hct:32.5%, Platlet:325K/mm³. Serum electrolytes (mEq/l): Na⁺ 140, K⁺ 4.3, Cl⁻ 107, HCO₃⁻ 30, corrected Ca⁺² for albumin 9.4, Cr 0.9 mg/dl, BUN 7 mg/dl, serum albumin 1gm/dl, total protein 4.5 gm/dl. Urinalysis: 4+ protein, 2-5 WBCs, no RBCs or casts. 24 hr urine protein was 8 gm/24 hrs. Serologies were negative for RPR, HIV, hepatitis B and C, Anti-DsDNA, Rheumatoid factor, C-ANCA, P-ANCA, and cryoglobulins. He had a positive ANA, and normal C3 and C4. SPEP and UPEP were negative for monoclonal proteins. Serum free light chain assay showed a normal free Kappa/Lambda ratio.

Kidney biopsy: Light microscopy showed mesangial and endothelial proliferation with basement membrane double contours. Immunofluorescence showed 3+ IgG granular capillary wall and mesangial deposits. 3+ Kappa light chains were present in a similar pattern; lambda light chains were negative. 1+ C3 deposits were present while IgA and C1q were negative. Electron microscopy showed mesangial and subendothelial electron dense deposits. Fibrillary deposits were absent. Biopsy diagnosis was MPGN with monoclonal IgG deposits.

Conclusion: A recent report (J Am Soc Nephrol 20:2055, 2009) described 37 patients with proliferative GN associated with monoclonal IgG deposition; 49% had nephrotic syndrome, 57% had MPGN, 30% were associated with paraproteinemia without progression to MM during follow up of 30 mos. Treatment of this condition has not been determined. Our patient is being treated with lisinopril, prednisone, and azathioprine. His urine protein has significantly decreased and renal function remains normal.

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CRESCENTIC GLOMERULONEPHRITIS IN A PATIENT WITH CROHN'S DISEASE: FIRST ASSOCIATION OF CROHN'S DISEASE AND RENAL WEGENER'S GRANULOMATOSIS

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Case Report: Background: Both Crohn's disease and Wegener's granulomatosis are chronic granulomatous inflammatory disorders with potential for multi-systemic involvement. We describe a patient with previously diagnosed Crohn's disease, who presented with acute renal failure and skin lesions and was diagnosed to have Wegener's granulomatosis. To our knowledge, this is the first report of renal involvement with Wegener's granulomatosis in a patient with Crohn's disease.

Case Report: A 33 year-old Caucasian man with a history of Crohn's disease was transferred to our medical center for evaluation and management of severe acute renal failure that required hemodialysis; renal biopsy revealed pauci-immune crescentic glomerulonephritis. Biopsy of the skin lesions suggested leukocytoclastic vasculitis. Serum titers for proteinase-3 anti-neutrophilic cytoplasmic antibodies (c-ANCA) were reported as > 100 U/mL (negative < 6). A diagnosis of Wegener's granulomatosis was made. Clinical course was complicated by a simultaneous polymicrobial bacteremia (S. maltophilia and A. xylosoxidans), secondary to an old vascular access device, limiting administration of immunosuppressive agents initially. Plasma exchange and trimethoprim-sulfamethoxazole therapy was instituted, with stabilization of renal function. Once bacteremia resolved, glucocorticoids and pulse intravenous cyclophosphamide were added to his regimen with further improvement.

Conclusions: Both Crohn's disease and Wegener's granulomatosis are chronic granulomatous inflammatory disorders with potential for multi-systemic involvement. The persisting infection of indwelling vascular access device may have contributed to acute exacerbation of vasculitis. While new symptoms in a patient could be explained by one unifying diagnosis, this case illustrates the need to consider additional diagnoses for these symptoms, so that appropriate therapy can be promptly initiated.

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THE ROLE OF NITRIC OXIDE IN THE URINE CONCENTRATION MECHANISM IN DIABETIC RATS

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Purpose of Study: Uncontrolled diabetes mellitus (DM) leads to osmotic diuresis and reduced urine concentration, frequently resulting in severe volume depletion. Nitric oxide (NO) is key for producing concentrated urine. Unfortunately, patients with DM have low levels of NO which may exacerbate polyuria. We examined how the absence of NO affects the transporters involved in urine concentration in a DM model.

Methods Used: Sprague Dawley rats were injected with streptozotocin (62.5 mg/kg) to induce DM. Control and DM rats were given NG(Nitroglycerin)-nitro-L-arginine methyl ester (L-NAME), a non-selective inhibitor of nitric oxide synthase, (50 mg/kg/d) for 3 wk. Urine osmolality, urine output and protein expression of the urea transporter UT-A1, water transporter AQP2 and Na-K-2Cl cotransporter NKCC2, were measured. Statistical analyses (ANOVA followed by Newman-Keuls) were performed for each cohort (n=3) where significance was p < 0.05.

Summary of Results: Urine osmolality was lower in DM rats, however in DM rats treated with L-NAME, levels were similar to untreated and L-NAME treated animals. L-NAME treatment did not change urine output however L-NAME treated DM rats produced less urine than untreated DM rats. L-NAME treatment did not alter UT-A1 protein abundance in inner medulla (IM). UT-A1 was increased in IM of DM animals. Interestingly, L-NAME-treated DM rats also had increased UT-A1 expression but the abundance was less than untreated-DM animals. AQP2 abundance was up in the IM of both DM and DM-L-NAME rats compared to the control group. L-NAME treatment had no effect on control or DM rat AQP2 expression. Similarly, NKCC2 expression was increased in both DM and L-NAME-treated DM rat outer medulla. L-NAME did not alter NKCC2 abundance compared to control or the DM untreated animal.

Conclusions: Increased protein expression of UT-A1, AQP2 and NKCC2 observed in DM rats provides a compensatory mechanism to decrease volume loss. Our data show that lack of NO prevents the increase of UT-A1 in DM but reduces urine osmolality and output. While the role of NO in the urine concentration mechanism remains unclear, alteration of NO levels may be beneficial in treatment of the osmotic diuresis occurring in DM.

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CORRELATION BETWEEN ROUTINE PERI-HEMODIALYSIS BLOOD PRESSURE MEASUREMENTS AND AMBULATORY BLOOD PRESSURE MEASUREMENT IN PATIENTS WITH END-STAGE RENAL DISEASE

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Purpose of Study: Nephrologists routinely use blood pressure (BP) measurements during hemodialysis (HD) to assess BP control in patients with End-Stage Renal Disease (ESRD) on dialysis. Our study objective was to assess correlation between routine pre/post BP values on HD and results on 48-hour ambulatory blood pressure monitoring (ABPM).

Methods Used: Forty-three patients were recruited from the University of Mississippi Medical Center Outpatient Hemodialysis Unit. Data obtained on age, race, gender, co-morbid illnesses (hypertension, congestive heart failure, diabetes mellitus), vintage on dialysis, last 6 previous dialysis logs and 48 hour ambulatory blood pressure measurements. Data are presented as either percentage or means with $\pm$ SD and analyzed with SPSS v.16. ANOVA and logistic regression analyzed the correlation between routine peri-HD BP with BP on ABPM. Data was also analyzed according to vintage (> or < three years of ESRD), age (> or < 65 years), or the presence of diabetes.

Summary of Results: Of the 43 participants, 19 (44%) were male, 41 (95%) African-American, 19 (44%) had diabetes and 41 (95%) patients had hypertension. Mean $\pm$ SD pre-HD BP was 164.6/87.9 mmHg (22.3; 15); post-HD 151.5/81.3 mmHg (24.1; 13). Mean ideal target weight was 85.4 (17.9) kg with mean interdialytic weight gain (IDWG) 2.01 kg (SD 0.93). On ABPM, systolic and diastolic BPs were similar irrespective of vintage, age, and diabetes. Vintage was associated with both pre and post-HD diastolic BP

(p 0.049 and 0.026, respectively) but only with systolic BP pre-HD (p 0.021). Average IDWGs correlated only with post-HD systolic BP (p 0.047). Statistical significant correlation existed between diastolic pre-HD BP, systolic and diastolic post-HD BP and average systolic and diastolic BP on ABPM (p 0.01, <0.001 and 0.037 respectively). Systolic BP on ABPM and pre-HD did not correlate. Post-HD BP maintained significance (p <0.001) using logistic regression.

Conclusions: Post-HD BP measurements correlate with ABPM measurements and should be used preferentially when assessing BP control in ESRD patients.

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DISRUPTION OF GUANYLYL CYCLASE-A/NATRIURETIC PEPTIDE RECEPTOR-A GENE CAUSES RENAL FIBROSIS AND HYPERTROPHY

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Purpose of Study: Atrial and brain natriuretic peptides (ANP and BNP) play an important role in maintaining renal function and cardiovascular homeostasis. Both ANP and BNP exert their biological actions through their membrane-bound receptor known as guanylyl cyclase-A/natriuretic peptide receptor-A (GC-A/NPRA). The objective of the present study was to evaluate the consequences of Npr1 gene (coding for GC-A/NPRA) disruption on renal fibrosis and remodeling in Npr1 null mutant mouse model.

Methods Used: In the present study, we utilized homozygous null mutant (Npr1^{-/-}), heterozygous (Npr1^{+/-}) and wild-type (Npr1^{+/+}) mice.

Summary of Results: The systolic blood pressure (SBP) was increased by almost 40 mmHg higher in null mutant homozygous mice (0-copy) as compared with the wild type (2-copy) mice. The systemic disruption of Npr1 gene caused an increase in the kidney weight/body weight (KW/BW) ratio in null mutant mice. The histological findings revealed an increased renal tubular damage as characterized by its dilation with flattened epithelium and expanded interstitial spaces. Furthermore, a significant increase occurred in pro-inflammatory cytokines including tumor necrosis factor- α (TNF- α) by 4-fold, interleukin-6 (IL-6) by 4.5-fold and increased induction of pro-fibrotic cytokine transforming growth factor- β 1 (TGF- β 1) by 2-fold. On the other hand, the present study demonstrated a decreased level of matrix metalloproteinase-9 (MMP-9) and an increased level of tissue inhibitor of MMP (TIMP-2) in the 0-copy mouse kidney. The renal collagen content was increased by 2-fold in 0-copy mice compared with wild-type mice. Moreover, we found an increased epithelial to mesenchymal transition (EMT) in the kidneys of 0-copy mice as reflected by increased expression of alpha smooth muscle actin (α -SMA) at both mRNA and protein levels.

Conclusions: Taken altogether, our results showed that systemic disruption of Npr1 activates the process of fibrosis and hypertrophic growth, which leads to impairment of renal functions and subsequent fibrosis in the kidneys of Npr1 null mutant mice.

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SERINE PROTEASE EFFECTS ON TRANSEPITHELIAL PERMEABILITY IN CORTICAL COLLECTING DUCT CELLS

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Purpose of Study: Proteolytic enzymes such as furin and prostaticin have been shown to activate epithelial Na channels (ENaC). Inhibition of apical serine proteases with aprotinin (apr) decreases Na current (I_{eq}), and subsequent application of the protease trypsin (tryp) increases I_{eq}. However, transepithelial resistance (R_{te}) also decreases with apr and increases with subsequent tryp; R_{te} effects are opposite to those expected with inhibition and activation respectively of ENaC. The present study directly addresses whether proteolytic enzymes have effects on R_{te} and transepithelial permeability.

Methods Used: Transepithelial voltage (V_{te}) and R_{te} were measured and I_{eq} calculated in M-1 cells cultured on permeable supports.

Summary of Results: Tryp had no effect on R_{te} in untreated M-1 cells unless endogenous proteases had been inhibited with apr. Since apr has effects on both I_{eq} and R_{te}, other experiments were performed to determine if effects on R_{te} required active Na transport. M-1 cells were treated with basolateral ouabain or apical amiloride (in the latter case after apical apr) to

inhibit I_{eq}. Subsequent addition of tryp significantly increased R_{te} in both cases even in absence of transport. These effects demonstrate that effects on Na transport and R_{te} are independent.

Recently the actions of proteases on Na transport have been postulated to be secondary to the release of inhibitory peptides from the alpha and gamma subunits of ENaC. To determine whether the inhibitory peptides are involved in the effects on R_{te}, synthetic inhibitory peptides were applied to the apical membranes of M-1 cells. Peptides LPHPLQRL (a-8) and PRFLNLIPLLVFNEN (γ -15) were synthesized by GenScript. Apical a-8 and γ -15 inhibited I_{eq} by 36% and 33% respectively compared to control after 30 minutes of application. However in contrast to the effects of tryp and apr, there was no effect on R_{te}. Subsequent apr decreased R_{te} by 62% and 50% respectively just as in control cells.

Conclusions: These results indicate that proteolytic enzymes including endogenous prostaticin alter Na transport in collecting duct cells both via the release of ENaC inhibitory peptides and in addition via the effects on R_{te}, probably reflecting paracellular permeability, independent of the effects on Na channels and Na transport.

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DYSNATREMIA IN PATIENTS WITH VENOUS THROMBOEMBOLISM

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Purpose of Study: Venous thromboembolism (VTE) and dysnatremia are frequently present in hospitalized patients, and are associated with increased morbidity and mortality. This study was designed to evaluate the frequency of dysnatremia (hypo- and hypernatremia) in patients with VTE, and to identify the factors contributing to development of dysnatremia.

Methods Used: Patients with documented VTE over a 2 yr period were identified (n=174). Data collected included demographics, biochemical parameters, and risk factors for VTE and dysnatremia. Serum Na⁺ level at the time of VTE diagnosis was defined as hyponatremia (< 135 mmol/l), normal Na⁺ (135–145 mmol/l) and hypernatremia (>145 mmol/l). There were only 5 hypernatremic patients and these were included in the normal Na⁺ group for statistical analysis. T test was used to compare the continuous variables and χ^2 test for categorical variables.

Summary of Results: VTE patients were 93% males and 50% were Caucasian. 40% had malignancy. 15% had serum Na⁺ < 135 mmol/l with 4% < 130 mmol/l. 82% had normal serum Na⁺, and 3% had hypernatremia. There were no significant differences between the 2 groups (<135 vs >135 mmol/l) in age, concentrations of creatinine, glucose, or BUN, hct, or platelet count. The WBC count was higher in the hyponatremia group. There were no significant differences between the 2 groups in VTE risk factors and associated comorbidities including: cancer, smoking, recent surgery, immobilization, recent travel, fracture, previous VTE, recent MI, proteinuria, or atrial fibrillation. More patients in the normal Na⁺ group had strokes. There were no significant differences between the 2 groups in diseases associated with hyponatremia including cirrhosis, systolic CHF, nephrosis, recent surgery, hypothyroidism, malignancy, or diuretic use.

Conclusions: Malignancy was the primary risk factor for VTE (40%). The incidence of hyponatremia defined as < 135 mmol/l or < 130 mmol/l, did not differ from previously reported series of hospitalized patients, 15%¹ and 3–4%², respectively. Hypernatremia was uncommon (3%). Despite common risk factors, there was no increased association between dysnatremia and VTE disease.

References:

1. Am J Med. 2009;857-65.
2. Semin Nephrol. 2009;227-38.

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THE MYSTERIOUS NEPHROPATHY

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Case Report: A 15 year old female was first noted to have mild proteinuria in January of 2008 at her pediatrician's office during a workup for abdominal pain. U/A showed 2+ protein and trace blood. She had normal renal function

and blood counts. 2 months later she was seen in our nephrology clinic for evaluation of proteinuria. Her physical exam was normal. Repeat U/A showed 1+ blood but was negative for protein. A 24 hour urine collection for protein was normal. Serological tests for C3, IgA, and ANA were normal. At that point the diagnosis of benign orthostatic proteinuria was suspected.

She was seen again in July of 2009 for a 2 month history of recurrent gross hematuria. Again her physical examination was normal with no evidence of SLE or other systemic illness. U/A was negative for blood and protein. A complete metabolic profile, urine calcium to creatinine ratio, C3 and IgA all were normal. Renal biopsy was consistent with mesangial IgG glomerulonephritis with exclusive mesangial IgG deposits.

Mesangial IgG Glomerulonephritis (MIG) is a very rare form of glomerulonephritis. The first cases of MIG were observed in Japan by Sato in 1993. In reviewing the limited amount of literature on MIG, there are clear contradictions among different studies. While Sato claimed the outcome is benign after a median follow-up period of 4.9 yr, a new study published in 2002 with a mean follow-up period of 11.5 yr showed the aggressive nature of MIG, inasmuch as chronic renal failure occurred in one-half of the patients. Also, it described the first recurrence of MIG in a renal graft. The incidence of MIG may be underestimated, because patients with mild urinary abnormalities do not undergo renal biopsies. The pathogenesis of MIG remains unclear and patients may present with nephrotic syndrome, microscopic or macroscopic hematuria and/or asymptomatic proteinuria. This previously healthy 15 year old female presented with mild intermittent proteinuria and recurrent hematuria. All clinical exams and other lab tests were normal. She was treated with supportive care and followed for progression of her symptoms. The renal biopsy was consistent with MIG. Pediatricians and pediatric nephrologists should be aware of this type of glomerulonephritis for its possible aggressive nature and poor outcome.

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DIRECT RENIN INHIBITION WITH ALISKIREN NORMALIZES BLOOD PRESSURE IN CYP1A1-REN2 TRANSGENIC RATS WITH INDUCIBLE ANG II-DEPENDENT MALIGNANT HYPERTENSION

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Purpose of Study: In Cyp1a1-Ren2 transgenic rats [strain name: TGR(Cyp1a1Ren2)], the induction of the Cyp1a1 promoter by dietary administration of the aryl hydrocarbon, indole-3-carbinol (I3C), drives hepatic expression of the Ren2 renin gene and results in the development of angiotensin (ANG) II-dependent hypertension. AT1 receptor blockade prevents the hypertension in this model; however, little information is available regarding the blood pressure and renal functional responses to direct inhibition of renin in this high circulating renin model of hypertension. The present study was performed to determine the effects of acute direct renin inhibition with aliskiren on blood pressure and renal hemodynamics in Cyp1a1-Ren2 transgenic rats with ANG II-dependent malignant hypertension.

Methods Used: Male Cyp1a1-Ren2 rats (n=6) were fed a normal diet containing 0.3% I3C for 9-11 days to induce malignant hypertension. Mean arterial pressure (MAP) and renal hemodynamics were measured in pentobarbital-anesthetized male Cyp1a1-Ren2 rats during control conditions and following administration of the renin inhibitor, aliskiren (10 mg/kg, iv).

Summary of Results: Rats induced with I3C had higher MAP (196 ± 4 vs. 142 ± 3 mmHg, $P < 0.01$) and lower renal plasma flow (RPF; 1.98 ± 0.32 vs. 3.86 ± 0.26 ml/min.g, $P < 0.01$) than non-induced rats (n=6). There were no differences in glomerular filtration rate (GFR) between the two groups (1.22 ± 0.13 vs. 0.85 ± 0.15 ml/min.g). Aliskiren administration decreased MAP (196 ± 4 to 126 ± 6 mmHg, $P < 0.001$) and increased RPF (1.98 ± 0.32 to 2.67 ± 0.46 ml/min.g, $P < 0.05$) in the hypertensive rats. GFR remained unaltered following renin inhibition in the hypertensive rats. Aliskiren administration did not alter MAP or GFR, but increased RPF (3.86 ± 0.26 to 4.53 ± 0.33 ml/min.g, $P < 0.05$) in the normotensive rats.

Conclusions: The present data demonstrate that acute renin inhibition with aliskiren normalizes MAP and improves RPF in Cyp1a1-Ren2 transgenic rats with malignant hypertension. The normalization of MAP and the increased RPF following acute renin inhibition with aliskiren indicate that renin generated as a consequence of expression of the Ren2 gene is responsible for the development of malignant hypertension and the associated reduction of renal hemodynamic function in Cyp1a1-Ren2 transgenic rats.

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RENOPROTECTIVE EFFECTS OF PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP) ON CYCLOSPORINE-INDUCED NEPHROTOXICITY IN MICE

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Purpose of Study: Cyclosporine A (CsA) is a widely used immunosuppressant drug for post-allogeneic organ transplantation. Major limiting factors in the use of CsA are its acute and long-term toxic effects on the kidney (nephrotoxicity). PACAP has been shown to protect the kidney from ischemic and nephrotoxin-induced renal injury in vitro and in vivo by modulating immune responses. This study evaluates the effects of PACAP38 in CsA-induced nephrotoxicity both in vitro and in vivo.

Methods Used: Male BALB/c mice (8–10 weeks) were given a single injection of CsA (5 mg/kg b.w.) intraperitoneally (i.p.). The treatment groups received 20 µg of PACAP38 2 hr before the CsA exposure and additional doses were given everyday for ten days. Control mice received equal volumes of saline i.p. for 10 days. HK-2 cells were cultured routinely and primary mouse renal proximal tubule cell cultures were generated from the isolated kidneys of mice.

Summary of Results: Exposure to CsA significantly stimulated the production of the profibrotic cytokine TGF-β1 in mouse kidneys and in cell cultures. Studies in vivo showed that PACAP38 treatment results in lower concentrations of kidney TNF-α and serum creatinine. PACAP38 significantly reduced renal tubular injury, inhibited the apoptotic cascade, and blocked epithelial-mesenchymal transition (EMT) of the renal cells as demonstrated by restoration of E-cadherin and ZO-1 and suppression of CsA-induced α-SMA and E2A. PACAP38 markedly suppressed the expression of MCP-1, IL-6, fibronectin, and TNF-α, and restored the expression of collagen IV, CXCL1, HIF1-α, IFN-γ, and TANK in CsA-exposed mice as demonstrated by real-time RT-PCR. Furthermore, PACAP38 also significantly reduced NADPH and angiotensin II in the kidney cortex of mice exposed to CsA.

Conclusions: We have demonstrated that the exposure to a clinically relevant dose of CsA provoked EMT in mouse kidney. PACAP38 effectively suppressed the EMT process and TGF-β1 production to prevent tubulointerstitial fibrosis both in vitro and in vivo. PACAP could be developed as a novel renoprotective agent for CsA-induced nephrotoxicity.

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TUMOR NECROSIS FACTOR-ALPHA (TNF-α) MEDIATES IT'S ACUTE RENAL VASOCONSTRICTOR AND NATRIURETIC RESPONSES VIA TNF-α RECEPTOR TYPE 1

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Purpose of Study: Recently, we reported that acute in-vivo infusion of TNF-α in mouse exerts a vasoconstrictor action but causes diuresis and natriuresis in the kidney. However, the roles of TNF-α receptor type 1 (TNFR1) and type 2 (TNFR2) in these renal vascular and tubular actions of TNF-α are not clearly defined. It has been reported that TNFR1 is abundantly present in renal glomeruli whereas TNFR2 is mainly located in the renal tubules. We hypothesize that TNF-α exerts its vascular action via TNFR1, while its tubular action is mediated by TNFR2. The purpose of the present study is to examine this hypothesis by evaluating renal responses to TNF-α in knockout mice that are lacking the gene for TNFR1 (TNFR1KO) and TNFR2 (TNFR2KO).

Methods Used: Experiments were conducted to assess the responses to intravenous infusion of human recombinant TNF-α (0.33ng/min/g BW for 75 min) in TNFR1KO (n=6) and TNFR2KO (n=6) mice and compared these results with those obtained in corresponding wild type (WT; C57BL/6) mice (n=6). Renal blood flow (RBF) and glomerular filtration rate (GFR) were determined by para-aminohippuric acid (PAH) and inulin clearances respectively. Concentrations of PAH and inulin in urine and plasma samples were determined by spectrophotometry. Sodium concentration in urine and plasma samples was determined by flame photometry.

Summary of Results: As reported previously, TNF-α infusion in WT mice resulted in decreases of $20 \pm 5\%$ ($P < 0.03$) in RBF, $40 \pm 2\%$ ($P < 0.003$) in GFR as well as increases in $83 \pm 27\%$ ($0.05 > P > 0.01$) in urine flow (V), $363 \pm 104\%$

($P<0.05$) in sodium excretion (UNaV) and $682\pm182\%$ ($P<0.003$) in fractional excretion of sodium (FENa). These renal responses were completely absent in TNFR1KO mice. TNF- α infusion in TNFR1KO mice resulted in non-significant changes in renal parameters (RBF; $8\pm22\%$; GFR, $-18\pm14\%$; V, $15\pm16\%$; UNaV, $-47\pm12\%$; FENa, $-10\pm29\%$). However, TNF- α infusion in TNFR2KO mice showed similar changes in renal parameters as observed those in the WT mice. The responses in TNFR2KO mice were as follows: RBF; $-22\pm10\%$ ($0.05>P>0.01$); GFR, $-36\pm7\%$ ($P<0.002$); V, $91\pm19\%$ ($P<0.007$); UNaV, $327\pm70\%$ ($P<0.01$); FENa, $559\pm99\%$ ($P<0.001$).

Conclusions: These data demonstrate that TNF- α receptor type 1, not the type 2, is involved in mediating acute renal vascular and tubular actions of TNF- α .

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CARDIOVASCULAR EFFECT OF JOB STRAIN ON YOUNG HEALTHY PROFESSIONALS

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Purpose of Study: To assess the effect of job strain and metabolic syndrome on blood pressure and cardiovascular damage, we enrolled 160 healthy young professionals.

Methods Used: Office blood pressure (OBP), ambulatory BP (ABP) and carotid intima media thickness (IMT) were measured yearly for four years. The Karasek job strain model groups: exposed, those with high psychological demands (PD) and low decision latitude (DL) and non-exposed, those with high PD and high DL. Body mass index (BMI), abdominal circumference (AbC), and systolic blood pressure (SBP) changes during physical and mental stress (PS, MS) were measured every year. Triglycerides (TG), LDL and HDL measured at year 1 and 4. Multivariable model, linear mixed effect for IMT was run with several covariables; exposed group, TG, LDL, HDL, BMI, AbC, ABP and OSBP, SBP changes during PS and MS.

Summary of Results: A linear mixed model was used to study IMT across visits to assess the interaction between exposure to stress and AbC. Secondary univariate associations between mean IMT and covariates were assessed with linear regression models performed separately for data at year 1 and 4. In the first model the only significant variable was BMI ($p=0.0308$). In the second one the exposed group variable interacted with AbC ($p=0.035$). Additional analysis at each level of exposure was done. The non-exposed group, showed no association of AbC with IMT ($p=0.9948$). The exposed group showed association of AbC with IMT ($p<0.0001$). The regression slope shows that for every unit increase in AbC there is an associated increase of 0.0026 unit IMT. The unadjusted analysis of the individual covariates with mean IMT showed that AbC was associated with mean IMT at visits 1 ($p=0.0007$) and 4 ($p=0.0036$). BMI showed a significant association with mean IMT at visits 1 ($p=0.0009$) and 4 ($p=0.0067$). Changes in ASBP and OSBP were not significantly associated with mean IMT at visit 1, but at visit 4 the association was ($p=0.029$ and $p=0.0038$) respectively.

Conclusions: In summary, the exposed population that increased weight gain OSBP and ASBP, during a four year follow up, showed an association with detrimental changes in the IMT. We found no association between the changes in lipid profile or SBP changes after PS or MS and the IMT.

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INSULIN SIGNALING IN ZSF RATS - EVIDENCE FOR ANGIOTENSIN-INSULIN CROSSTALK

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Purpose of Study: Both experimental and clinical data support the notion that inhibition of angiotensin (Ang II) is associated with not only improvement of glycemic control in diabetics but also primary prevention of new onset diabetes. However our understanding of Ang II-insulin interactions is still evolving. Earlier in vitro studies in our laboratory suggested that Ang II inhibition had a modest salutary effect on insulin secretion by pancreatic islet beta cells. Because the major effect of angiotensin may be on peripheral insulin sensitivity, we hypothesized that Ang II interferes at multiple steps within the insulin signaling pathway and we investigated the Ang II -insulin crosstalk in ZSF rats, a newly characterized rat model of type II diabetes and metabolic syndrome and an excellent model to study

insulin resistance. Initial studies showed that Ang II blockade increased the expression of adiponectin receptors, which may increase insulin sensitivity.

Methods Used: In the current studies, we examined the effect of angiotensin blockade on glucose transporter 4 (GLUT4) and insulin receptor substrate 1 (IRS 1). ZSF rats were acquisitioned in 7th week and fed on high calorie diet to maintain hyperglycemia. The effects of Ang II were examined by administering losartan (25 mg/L in drinking water), an Ang II receptor blocker from 8–20th week. Lean ZSF rats were used as additional controls. Rats were euthanized at 20th week and homogenates of harvested skeletal muscle were examined for the expression of GLUT4, IRS1, phospho-serine IRS1 and phospho-tyrosine IRS1 proteins using immunoblotting with specific antibodies. The expression of these proteins was quantified using densitometric image analysis software and the ratio of phospho-serine IRS-1 to phosphotyrosine IRS1 was calculated. Our results show that obese rats were hyperglycemic and losartan administration improved the glycemic indices.

Summary of Results: Obese rats have diminished expression of GLUT4 and IRS1 proteins compared to their lean counterparts. Losartan increased the expression of these proteins. Furthermore losartan specifically increased the tyrosine phosphorylation of IRS1.

Conclusions: Ang II inhibition improved insulin resistance by rectifying many defects in insulin signaling pathway that characterize type II diabetes.

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STERILE INTRAPERITONEAL CATHETERS RESULT IN PROGRESSIVE INFLAMMATION IN MICE

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Purpose of Study: Polymer discs implanted intraperitoneally (ip) in mice are populated with inflammatory cells within 18 hours, but inflammation in peritoneal tissue has not been studied. Our hypothesis is that sterile, intraperitoneal polymer catheters will result in local inflammatory changes.

Methods Used: To address the hypothesis, we inserted intraperitoneally (ip) into each of 28 C57Bl/6 mice 5 sterile loops of catheter material made from medical-grade silicone for periods of 1, 2, 4, 5 weeks (E1, E2, E4, E5). Control animals (CON, n=12) underwent sham operations without catheter implantation. After 1–5 weeks, the animals were anesthetized and catheters were removed from the abdomen. The abdomen and adherent cell layer (ACL), after separation from the catheter, were cultured to demonstrate sterility. Transport experiments to determine the mass transfer coefficient of mannitol (MTCm), the osmotic flux (J_{osm}), and the albumin flux (J_{alb}) were carried out with chambers affixed to the abdominal wall. After animal sacrifice, samples of abdominal wall were studied with immunohistochemistry (IHC) for cytokines, and immunocytochemistry (ICC) was used to determine cell markers in the ACL.

Summary of Results: All cultures were negative indicating sterility of the ACL and mouse abdomens. Marked changes were noted in thickness (μm : CON, 18.8 ± 12.3 ; E1, 46.1 ± 20.0 ; E2, 72.0 ± 17.9 ; E4, 97.3 ± 20.0 ; E5, 131.7 ± 10.3 ; $p<0.003$) and angiogenesis in the peritoneum (#ves/mm: CON, 10.7 ± 9.4 ; E1, 15.4 ± 15.6 ; E2, 27.0 ± 14.0 ; E4, 39.8 ± 15.7 ; E5, 90.1 ± 8.1 ; $p<0.0003$). IHC for TGF β , FGF, VEGF, and α SMA showed staining that was 2.5–4x that of controls and demonstrated progression to denser stain versus time with α SMA and VEGF ($p<0.002$). ICC analysis of the ACL demonstrated macrophages (F4/80), dendritic cells (CD3), lymphocytes (CD8), mesothelial cells (cytokeratin), myofibroblasts (α SMA, vimentin). Transport studies demonstrated no significant changes in MTCm (mean of .0039 cm/min), but significant elevations of J_{osm} for E1–E5 (mean of .0018 cm/min) vs CON (.0013, $p<0.03$) and J_{alb} E1–E5 (mean .00018 cm/min) vs CON (mean .00015, $p<0.0001$).

Conclusions: The hypothesis was upheld: sterile silicone catheters in the cavity of mice induce peritoneal inflammation with alteration of structural and transport properties over 1–5 weeks.

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EFFECTS OF SPIRONOLACTONE IN SUBJECTS WITH RESISTANT HYPERTENSION AND STAGE III CHRONIC KIDNEY DISEASE

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Purpose of Study: Aldosterone blockade is effective in the management of advanced heart failure and resistant hypertension but is not widely used in subjects with advanced chronic kidney disease (CKD) because of the risk of hyperkalemia.

Methods Used: We retrospectively reviewed our Hypertension Clinic database to evaluate the efficacy and safety of spironolactone added to a pre-existing antihypertensive regimen that included a diuretic and a renin angiotensin system (RAS) inhibitor in subjects with resistant hypertension and stage III CKD (estimated glomerular filtration rate (eGFR) 30–59 ml/min/1.73 m²). Demographics, laboratory and medication data were extracted from the medical records for baseline and most recent follow-up visits. The primary end-point was change in systolic blood pressure (SBP). Secondary end-points included serum potassium and creatinine, eGFR, diastolic blood pressure (DBP), and tolerability. Statistical analysis was performed using paired t-test.

Summary of Results: Twenty-six patients started spironolactone between 10/22/03 and 05/15/09 and were included in the analysis. Spironolactone mean dose was 24±11 mg/day; median follow-up was 231 days. Mean age was 61±10; males were 69%, African-American 65%, and diabetics 31%. Mean body mass index (BMI) was 32±7 and the mean number of antihypertensive agents was 5±2. Spironolactone induced a significant decrease in SBP from 160±22 to 137±14 mmHg ($p<0.00003$). Serum potassium increased from 4.0±0.3 to 4.3±0.3 mEq/l ($p<0.005$), with the highest value being 5.7 mEq/l. Serum creatinine increased from 1.7±0.3 to 1.9±0.6 mg/dl ($p<0.003$) and eGFR decreased from 47.4±8.0 to 42.0±12.0 ml/min/1.73 m² ($p<0.009$). DBP decreased from 89±18 to 75±12 mmHg ($p<0.00002$). One patient developed acute renal failure that completely recovered once spironolactone was discontinued. One patient developed symptomatic hypotension that required spironolactone withdrawal. Two patients developed breast tenderness that resolved when spironolactone was discontinued.

Conclusions: Spironolactone significantly reduced blood pressure in subjects with resistant hypertension and stage III CKD. Treatment with spironolactone was generally safe and well tolerated although there was one case of acute renal failure highlighting the need for close monitoring.

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CHRONIC KIDNEY DISEASE, RISK OF CARDIAC ARREST, AND MYOCARDIAL FIBROSIS

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Purpose of Study: Patients with Chronic Kidney Disease (CKD) exhibit disproportionate risk of cardiac disease and are at progressively higher likelihood of dying from sudden cardiac arrest (SCA). Studies have shown that myocardial fibrosis (scar) is predictive of life-threatening arrhythmias in the general population, and cardiac MRI (CMRI) has been shown to accurately quantify scar. Recent studies suggest that myocardial scar is prevalent in patients with CKD, even in the absence of coronary artery disease (CAD). We sought to understand the relationship between estimated kidney function and myocardial scar burden.

Methods Used: Retrospective data from 135 patients undergoing ICD placement and concurrent CMRI at our institution were analyzed. Scar burden was defined as percent of left ventricular mass infarcted on CMRI. Estimated GFR (eGFR) at time of CMRI was determined, and coronary history reviewed. Multivariable linear regression was used to determine the relationship between eGFR and the extent of myocardial scar quantified on CMRI.

Summary of Results: In our 135 pts: 62% were male, the mean creatinine was 1.4 mg/dl, mean MDRD eGFR was 68.1 ml/min/1.73m², median age was 64yrs, 23.7% had diabetes, 49.6% had hypercholesterolemia, 54.1% had hypertension, and 54.8% had known CAD. These patients were divided into tertiles of eGFR (>80, 57–80, <57 ml/min/1.73m²), and the lowest tertile had significantly more hypertension (73.3%, $p=0.005$) and diabetes (37.8%, $p=0.024$). Additionally, when grouped in tertile by extent of scar, the use of antiplatelet agents, loop diuretics, and lipid lowering agents showed significant differences. In a multivariable model, using scar burden as the independent variable, there was significant interaction for eGFR ($p=0.0486$), number of vessels with >70% stenosis ($p=0.0064$), and history of myocardial infarction (MI, $p<0.0001$).

Conclusions: Although degree of myocardial scarring is a potent predictor of ventricular arrhythmias in the general population, in this cohort we found that decreasing GFR was independently associated with decreasing scar burden. This suggests that non-conventional factors, distinct from processes

that induce myocardial fibrosis, play a role in the observed increased risk of arrhythmias and SCA in patients with CKD. Further study is needed to elucidate these factors.

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SEXUAL DIMORPHISM OF INTRARENAL RENIN ANGIOTENSIN SYSTEM: ANGIOTENSINOGEN, RENIN AND ANGIOTENSIN II IN SPRAGUE-DAWLEY(SD) RATS DURING HIGH SALT DIET

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Purpose of Study: Coordinated actions between proximal tubule-derived angiotensinogen (pt-AGT) and renin produced by the principal cells of the collecting ducts (CD) may contribute to intrarenal Angiotensin II (Ang II) formation. Whether the responses of these RAS components to high salt (HS) differ between male and female rats, thereby explaining sexual dimorphism of renal injury, remains unclear.

Methods Used: Male (n=10) and female (n=9) SD rats fed normal salt (NS) or 8% NaCl high salt (HS) diet for 14 days were assessed for changes in systolic blood pressure (SBP) and proteinuria. AGT and renin gene expression were examined by real time qRT-PCR and Western blot in renal cortex and medullary tissues, respectively. Twenty four hour urine collections were used to determine proteinuria (Bradford protein assay), AGT (ELISA), and renin and Ang II levels (RIA).

Summary of Results: SBP in males and females were comparable and did not increase with HS. Proteinuria was earlier and greater in male than female rats fed HS. During NS diet, AGT and CD renin mRNA levels were higher in males than females: [AGT (male: 1.0±0.05; female: 0.2±0.1; $p<0.001$); CD renin (male: 1.0±0.4; female: 0.2±0.06 $p<0.001$)]. HS diet did not exert any effect on AGT mRNA levels; however, CD renin mRNA and protein levels of prorenin, but not renin, significantly increased in females but not males. [Renin mRNA (male HS: 1.1±0.1; female HS: 2.5±0.4, $p<0.001$); Prorenin protein (male HS: 0.4±0.3; female HS: 3.1±0.4). HS increased urinary renin in male and female rats [NS (male: 1±0.1; female: 1±0.2); HS (male: 7±1; female: 5.3±1 enzyme units; $p<0.05$)]. Although, urinary AGT was significantly higher in males than in females, HS did not exert further stimulation for either sex (male NS: 60±26; female 4.5 ±0.2 ng/mL/day, $p<0.05$). Ang II urinary excretion was greater in male than in female rats but did not change with diet (male NS: 2080±361; female NS: 1080±127 fmol/day; $p<0.05$).

Conclusions: Augmented pt-AGT and urinary Ang II levels may predispose male rats to more severe kidney injury.

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COMPARISON OF TIME TO BACTEREMIA IN HIV INFECTED HEMODIALYSIS PATIENTS FROM THE 1996 AND 2004 USRDS DATASETS

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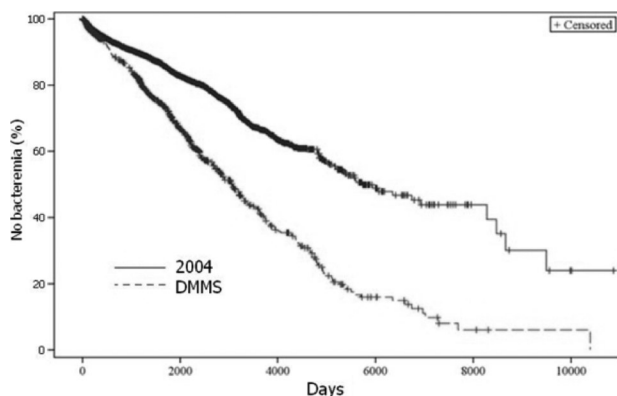
Purpose of Study: Bacteremia (BAC) is an important cause of morbidity and mortality in hemodialysis (HD) pts. We have previously queried the USRDS and shown that HIV is a risk factor for BAC in HD patients from both the DMMS (1996) and 2004, and that the rate of BAC significantly declined from 1996 to 2004 (JASN, in press).

Methods Used: These studies investigated the time to BAC for each cohort and compared the difference using survival curves.

Summary of Results: The number of HIV(+) pts on dialysis were 1,061 and 9,886 for 1996 and 2004, respectively. When compared to 1996, 2004 demonstrated a significant decrease in the rate of BAC (33.9% vs 16.4%, $p<0.0001$). Using the log-rank statistic, there was a difference between patients from DMMS and 2004 with respect to time to BAC ($p<0.0001$). Time to BAC for each pt was determined by calculating the number days between the start of HD and the first BAC episode in each time period. Survival curves for the time to BAC for the two cohorts are shown (figure) and indicate that the median times to infection were 3073 days (95% C.I. 2781,

3311) and 5726 days (95% C.I. 5335, 8276) for the DMMS and 2004, respectively. Of those that were infected, 75% were infected within 4911 days in DMMS and within 9500 days in 2004.

Conclusions: The rate of BAC in HIV(+) HD pts improved from 1996 to 2004, and this change is reflected by a significantly longer time to BAC in 2004.



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VASCULAR PATHOLOGY IN ANGIOTENSIN II-DEPENDENT HYPERTENSION DOES NOT DEPEND ON ACTIONS OF TYPE 1 ANGIOTENSIN RECEPTORS IN VASCULAR SMOOTH MUSCLE CELLS

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Purpose of Study: The renin angiotensin system promotes hypertension and vascular disease, including medial hypertrophy of conduit vessels such as the aorta. These actions are primarily mediated by type I angiotensin (AT_1) receptors. AT_1 receptors are expressed in a number of tissues including VSMCs where they may influence BP control and vascular pathology. However, it has been difficult to discriminate contributions of AT_1 receptor in specific cell lineages, such as VSMCs, in hypertension and end-organ damage using pharmacological inhibitors or gene targeting approaches. Accordingly, we developed an experimental model to study the role of AT_1 receptor in VSMCs *in vivo*, in isolation.

Methods Used: Using Cre/loxP technology, we generated a mouse line with a conditional allele of the *Agr1a* gene encoding the AT_{1A} receptor, the major murine AT_1 receptor. Expression of AT_{1A} receptors in VSMCs was eliminated by crossing the *Agr1a^{flax}* mice with a line expressing Cre recombinase under control of the Sm22 α promoter, which drives Cre expression in smooth muscle cells.

Summary of Results: Using RT-PCR, AT_{1A} mRNA could not be detected in aortae from Sm22 α -Cre⁺*Agr1a^{flax/flax}* SM-KO mice and was reduced by $\approx 60\%$ in mesenteric arteries compared to controls. By contrast, there was robust expression of AT_{1A} mRNA in isolated pre-glomerular arterioles from SM-KOs that was similar to controls. *Ex vivo* contractile responses to ang II were reduced by $\approx 75\%$ in the abdominal aorta and $\approx 65\%$ in the mesenteric arteries, but acute vasoconstrictor responses to ang II *in vivo* were similar in SM-KOs and controls. Baseline BPs were identical in SM-KO and control mice. During chronic infusion of ang II, SM-KOs and controls both developed significant hypertension with similar levels of BP elevation. Despite the absence of AT_{1A} receptors in aortic VSMCs, SM-KOs developed robust medial hypertrophy of the aorta that was not significantly different from controls.

Conclusions: In ang II-dependent hypertension, direct actions of AT_1 receptors in VSMCs contribute little to the development of vascular pathology in the aorta. Instead, other factors, such as the extent of BP elevation, may determine vascular injury.

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ACHIEVING BLOOD PRESSURE GOALS IN HIGH RISK PATIENTS WITH DIABETIC NEPHROPATHY

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Purpose of Study: Clinical practice guidelines recommend lowering blood pressure (BP) and inhibiting the renin-angiotensin system (RAS) to slow kidney disease progression in patients with diabetic nephropathy. Achieving target BP and maximal RAS inhibition remain challenging, particularly in vulnerable populations. This study's purpose was to determine whether an antihypertensive regimen including a maximally-dosed angiotensin converting enzyme inhibitor (ACEi) could safely achieve target BP and lower albuminuria in indigent, high-risk predominantly minority patients with diabetic nephropathy.

Methods Used: We studied 81 adults (52% Hispanic, 31% African American) with type I or type II diabetes, hypertension, and persistent albuminuria during the run in period of a completed randomized controlled trial. Subjects received lisinopril titrated to 80 mg daily and additional antihypertensives to achieve a systolic BP (SBP) < 130 mmHg. BP and serum potassium were measured weekly, and a 2g sodium diet was encouraged. This study's primary outcome was BP change from screening to randomization. Change in urine albumin to creatinine ratio (UACR) and ability to achieve goal SBP were also analyzed.

Summary of Results: Median SBP was 144 mmHg at screening and 133 mmHg at randomization with a median change of -9.6% (25th, 75th percentile: -15.8% , 0%). Thirty-four subjects (42%) achieved goal SBP at the randomization visit, and 58 (72%) achieved this during run in. Median UACR decreased from 1828 to 996 mg/g from screening to randomization with a median change of -42.7% (-61.8% , -13.3%). UACR reduction correlated with SBP reduction. Hyperkalemia (potassium ≥ 5.0 mEq/L) responsive to dietary or medical management occurred in 33 subjects, and 2 subjects had hypotension (SBP less than 100 mmHg) responsive to medication adjustments.

Conclusions: A strategy employing maximally-dosed lisinopril with additional agents is safe and effective for achieving significant reductions in BP and albuminuria in indigent patients with diabetic nephropathy. The majority of our subjects reached the recommended SBP target on this regimen. Serum potassium should be monitored regularly during lisinopril titration.

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PERCEIVED DISEASE SPECIFIC KNOWLEDGE IS LIMITED IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Purpose of Study: Patient knowledge about chronic kidney disease (CKD) is an important factor in the execution of successful disease self-care. Data concerning the understanding and perceived knowledge regarding treatment options for CKD in patients seen by nephrologists are scarce. The aim of this study is to characterize perceived kidney disease knowledge in areas specific to preventing CKD progression, including blood pressure targets, nephrotoxins, and warning signs of kidney failure.

Methods Used: Two-hundred established adult patients with CKD (Stages 1–5), seen at least once previously in the Nephrology clinic, were enrolled from May to July 2009. They were asked about awareness of their diagnosis ("Do you have chronic kidney disease?") and rated their CKD knowledge on a scale from 1 (No knowledge) to 4 (A lot of knowledge) in nine areas. The knowledge ratings were averaged to generate an overall perceived knowledge score. Health literacy was measured with the Rapid Estimate of Adult Literacy in Medicine survey.

Summary of Results: The mean age of this cohort was 57.3 years (SD 15.9), 83% were White, and 75% had CKD Stage 3–5. Low literacy (<9th grade level) occurred in 17%. 30% were unaware they had CKD. Most patients reported knowing little or nothing about medications beneficial (72%) or toxic (64%) to the kidney, the nutritional requirements of CKD (64%), treatment options (51%), symptoms of kidney failure (64%), and physiologic roles of the kidney (53%). Lower overall perceived knowledge scores were associated with older age [$\rho = -0.35$; $p = 0.01$], less education [mean(SD): < high school 2.24 (0.62) vs. > high school 2.63 (0.62); $p = 0.01$], lower health literacy [<9th grade 2.30 (0.66) vs. $\geq$ 9th grade 2.56 (0.61); $p = 0.03$], milder stages of CKD [Stage 3: 2.42 (0.61) vs. Stage 5: 2.90 (0.64); $p = 0.01$], and lack of previous attendance in a kidney education class [No 2.45 (0.60) vs. Yes 2.90 (0.59); $p = 0.01$]. Sex and race were not associated with overall perceived knowledge in this cohort.

Conclusions: Established CKD patients, especially those with less advanced CKD, seen in a nephrology clinic, report low perceived knowledge

about most of the areas of CKD self-care. Low health literacy may be a barrier to effective patient-provider communication about kidney disease care.

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PERFORMANCE OF ESTIMATING EQUATIONS FOR GLOMERULAR FILTRATION RATE IN CHRONIC SPINAL CORD INJURY PATIENTS WITHOUT CHRONIC KIDNEY DISEASE

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Purpose of Study: K/DOQI guidelines emphasize the importance of staging the severity of chronic kidney disease (CKD) using estimating equations for GFR (simplified MDRD and Cockcroft-Gault equations). A new equation developed by CKD-EPI researchers using data on more than 8,000 patients from 10 studies is reported to be more accurate than the MDRD equation, especially at higher GFR. However, none of these estimating equations have been validated in spinal cord injury (SCI) patients with muscle atrophy. We previously reported MDRD, CG and CKD-EPI equations overestimate GFR, as compared to 24hr creatinine clearance (mCcr), at all stages of CKD in SCI patients (J Inv Med 53: S330, 2005 and ASN 2009), and that accuracy and precision was improved by applying a correction factor. The present study was designed to evaluate estimates of GFR (eGFR) using the simplified MDRD and CKD-EPI equations, as compared to mCcr, in chronic SCI patients without CKD.

Methods Used: Review of medical records of 426 chronic SCI patients with measurements of 24 hr urinary creatinine clearance identified 104 patients with mCcr > 90 mL/min/1.73m². The simplified MDRD and CKD-EPI equations were used to calculate eGFR.

Summary of Results: Linear regression analysis relating eGFR to mCcr showed a very poor correlation between mCcr and eGFR using both equations, (CKD-EPI, $r = 0.33$, $p < 0.05$; Simplified MDRD, $r = 0.31$, $p < 0.05$). Correlations were slightly better in paraplegics than quadriplegics. Fractional Percentage Error for MDRD equation and CKD-EPI equations were 89% and 45%, respectively. A correction factor to improve accuracy and precision could not be generated because of the wide distribution of the values.

Conclusions: CKD-EPI equation appears to be more accurate than the simplified MDRD equation at higher GFRs in the normal population. However, in chronic SCI patients without CKD both equations are inaccurate. Therefore, continued measurement of creatinine clearance with timed urine collections is needed in this patient population.

**Southern Society for Clinical Investigation and Southern American Federation for Clinical Research
Plenary Session**

SSCI Young Investigator Award Finalists
SAFMR/SSCI/ Young Faculty Award
SAFMR/SSCI/ Trainee Research Award
8:00 AM
Friday, February 26, 2010

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DISRUPTION OF TRANSFORMING GROWTH FACTOR β (TGF β) SIGNALING BLOCKS PRESSURE OVERLOAD-INDUCED DOWNREGULATION OF ENDOGENOUS PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR γ (PPAR γ) EXPRESSION IN HEART

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Purpose of Study: PPAR γ activators modulate extracellular matrix (ECM) molecules expression in cardiac fibroblasts (CFs), which could attenuate myocardial fibrosis in the pressure overloaded heart. This study utilized a transgenic mouse model that expresses an inducible dominant negative mutation of the TGF β type II receptor (DnTGF β RII) to test the hypothesis that

PPAR γ expression is reduced in the pressure overload heart and that TGF β signaling is required for the pressure overload-induced down-regulation of PPAR γ expression.

Methods Used: 1) In vivo: 10 wk old male DnTGF β RII and nontransgenic (NTG) mice were given 25 mM Zn⁺⁺ in drinking water 1 wk prior to transverse aortic constriction (TAC) to induce expression of the DnTGF β RII gene. PPAR γ protein levels in left ventricles (LV) were assessed 1 wk after TAC. 2) In vitro: Mouse CFs were transfected with a PPAR γ promoter+ luciferase reporter plasmid and exposed to TGF β 1 (1 ng/ml) for 24 hrs. PPAR γ promoter activity, mRNA and protein levels were assessed. Chromatin immunoprecipitation (ChIP) assay was used for detection of binding of Smad proteins and a transcriptional co-repressor and co-activator on the PPAR γ promoter.

Summary of Results: TAC decreased LV PPAR γ protein levels in TAC-NTG mice. In contrast, PPAR γ protein levels were increased in LV of DnTGF β RII mice when TGF β signaling was disrupted. TGF β 1 treatment decreased PPAR γ promoter activity ($\downarrow$ 53%), mRNA ($\downarrow$ 34%) and protein ($\downarrow$ 52%) levels in CFs. Activation of TGF- β signaling significantly increased binding of Smad2/3, Smad4 and histone deacetylase-1 (HDAC1, a transcriptional co-repressor), and decreased binding of acetylated histone 3 (AcH3, a transcriptional co-activator) to the promoter region of the PPAR γ gene.

Conclusions: These data indicate that TGF β 1 enhances Smad2/3/4 binding to the PPAR γ promoter and that this coincides with increased HDAC-1 and decreased AcH3 binding, as well as decreased expression of the PPAR γ gene in CFs. The finding that TGF β 1 can directly suppress PPAR γ expression in CFs via a transcriptional mechanism suggests that inhibition of PPAR γ expression may be a novel mechanism of TGF β -mediated cardiac fibrosis.

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OXIDATIVE STRESS, MITOCHONDRIAL PERMEABILITY TRANSITION PORE OPENING AND CARDIAC HYPERTROPHY WITH FIBROSIS IN ALDOSTERONISM: RESPONSE TO SUPPLEMENTAL ZINC

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Purpose of Study: Aldosterone/salt treatment (ALDOST) leads to secondary hyperparathyroidism (SHPT) with parathyroid hormone-mediated intracellular Ca²⁺ overloading and the induction of oxidative stress in cardiomyocytes and mitochondria with opening of the mitochondrial permeability transition pore (mPTP), which eventuates in necrosis with subsequent scarring. Concomitantly, Zn²⁺-based antioxidant defenses are reduced. We hypothesized a Zn²⁺ supplement would ameliorate the prooxidant:antioxidant imbalance and prove cardioprotective.

Methods Used: Eight-wk-old uninephrectomized rats received 4 wk ALDOST alone or with ZnSO₄ cotreatment (40 mg/day; gavage) and were compared to unoperated/untreated age-/sex-matched controls (n=6/group). We monitored: arterial pressure; echocardiographic ventricular function; fibrosis by histochemistry; cardiomyocyte size by planimetry and hypertrophy by myosin heavy-chain (MHC- α and - β) and pro-atrial natriuretic peptide (ANP) mRNAs; biomarkers of oxidative stress, including mitochondrial H₂O₂ production; mPTP opening; and endoplasmic reticulum (ER) stress by BiP/GRP78 and protein disulfide isomerase (PDI) using RT-PCR and immunoblotting.

Summary of Results: Compared to ALDOST alone, ZnSO₄ cotreatment: attenuated ($p < 0.05$) scarring and the rise in collagen volume fraction (4.79 ± 0.87 and $3.89 \pm 0.34\%$, respectively, vs. controls $2.22 \pm 0.04\%$); improved depressed ($p < 0.05$) fractional shortening seen with ALDOST (53 ± 2 vs. $42 \pm 5\%$ and controls $46 \pm 2\%$), without preventing hypertension or compensatory hypertrophy; reduced ($p < 0.05$) oxidative stress, including mitochondrial H₂O₂ production and ER stress while preventing mPTP opening. Furthermore, ZnSO₄ cotreatment attenuated upregulation of MHC- β , a marker of pathologic hypertrophy.

Conclusions: In the hypertrophy that accompanies the SHPT of aldosteronism, the induction of oxidative stress, coupled with mPTP opening, ER stress and reduced antioxidant defenses, contribute to cardiomyocyte necrosis and scarring with reduced shortening. This prooxidant phenotype

can be overcome by fortifying the heart's antioxidant capacity with a Zn²⁺ supplement.

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ABSENCE OF SPHINGOSINE KINASE 1 INHIBITS JOINT EROSIONS IN TNF- α INDUCED ARTHRITIS

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Purpose of Study: Sphingolipids, constituents of the plasma membrane, can alter cellular functions. Sphingosine 1 phosphate (S1P) in vitro is required for TNF α induced COX-2 and PGE2 production while, stimulation with TNF α and S1P leads to more COX-2 and PGE2 than either alone. Both sphingosine kinase (SphK) 1 and 2 are upregulated in rheumatoid synovium compared to osteoarthritis synovium. Additionally, S1P1R, an S1P receptor, is upregulated in RA patients. Fibroblast-like synoviocytes (FLS) proliferate with proinflammatory cytokines and produce COX-2 and PGE2 with TNF α and S1P. We hypothesized that S1P, induced by TNF α is a critical mediator of inflammation and joint damage in the rheumatoid joint.

Methods Used: The following experiments were performed to test this hypothesis: Transgenic hTNF α mice were crossed with SphK1^{-/-} mice and genotyped by PCR. Arthritis in these mice develops independent of antigen, T cells or B cells. The mice were observed weekly for disease activity, while CT images and microarray analysis were used to evaluate disease activity in the joint and evaluate genetic profiles respectively.

Summary of Results: hTNF/SphK1^{-/-} mice (n=15) had significantly decreased clinical joint disease compared to hTNF/SphK1^{+/+} mice (n=18), with average arthritis scores of 1+/-0.5 vs. 5+/-1.2 respectively at 5 months (based on joint swelling and deformity). An erosion Index, measured quantitatively from 3D CT images of the ankles was significantly decreased in hTNF/SphK1^{-/-} mice at 4 and 5 months, with a 2 fold decrease in erosions in hTNF/SphK1^{-/-} vs. hTNF/SphK1^{+/+} mice. Microarray analysis of ankle joint synovium, with RT-PCR confirmation, demonstrated significant modulation of a cluster of genes regulated by SOCS3 in hTNF/SphK1^{-/-} mice compared to hTNF/SphK1^{+/+} mice.

Conclusions: Genetic deletion of SphK1 significantly decreased the severity of hTNF α induced arthritis, decreased erosions and led to upregulation of SOCS3 with impact on expression of SOCS3 related genes. These data indicate that S1P plays a key role in TNF α induced joint inflammation and erosions and is a potential target for therapeutic intervention in inflammatory arthritis.

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LOW SERUM INSULIN-LIKE GROWTH FACTOR 1 POTENTIATES ATHEROCLEROTIC PLAQUE DEVELOPMENT IN APOE KNOCKOUT MICE: POTENTIAL MECHANISM OF ACCELERATED ATHEROSCLEROSIS IN AGING

S. Shai, Y. Higashi, S. Sukhanov, P. Delafontaine *Tulane Univ. School of Medicine, New Orleans, LA.*

Purpose of Study: Aging is associated with a reduction in serum insulin-like growth factor-1 (IGF-1) levels and an increased risk of atherosclerosis, but whether lower IGF-1 plays a causative role is unknown. This study is aimed to obtain insights into the relation between circulating IGF-1 levels and atherosclerotic burden independent of age.

Methods Used: A congenic mouse strain with a 20% reduction in circulating IGF-1 (C3H.B6-6T [6T]) was bred into the ApoE knockout (ApoE KO) background to obtain the C3H.6T^{+/+}/ApoE KO (6T/E) mouse to mimic the clinical state of low circulating IGF-1 and to study its effect on atherosclerosis development.

Summary of Results: Serum IGF-1 levels in 6T/E mice were similar to those of 6T (6T/E: 208.81 $\pm$ 58.33 ng/ml vs 6T: 221.41 $\pm$ 58.33 ng/ml, p=0.6); but lower than those of ApoE KO (354.49 $\pm$ 76.33 ng/ml, p<0.01). Mice of all 3 groups (6T/E, 6T and ApoE KO) at 8 weeks old were fed with normal chow (NC) or western diet (WD) for 12 weeks and en face whole aortas were stained with Oil Red O. Results showed that (1) the NC-fed 6T/E mice developed more plaques than ApoE KO mice (% total plaque/aorta,

6T/E: 7.54 $\pm$ 2.21, ApoE KO : 4.91 $\pm$ 3.18, p<0.018); (2) when fed with the WD, the 6T/E also developed more plaques than the ApoE KO (6T/E: 14.87 $\pm$ 8.81, ApoE KO : 8.71 $\pm$ 3.13, p=0.0005). (3) There was no difference in body weight gain or blood pressure between the 6T/E or ApoE KO mice.

Conclusions: A novel atherosclerosis-prone mouse model that mimics age-related low circulating IGF-1 levels has been created. In these mice, a decrease in serum IGF-1 is accompanied by a diet-independent increase in aortic atherosclerosis. These results are consistent with epidemiological data indicating that lower IGF-1 levels are associated with an increased risk for ischemic heart disease and strongly support the rationale for development of new IGF-1-based therapies against atherosclerosis.

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REPETITIVE BLEOMYCIN LUNG INJURY RESULTS IN HYPERPLASTIC ALVEOLAR EPITHELIAL CELLS AND INCREASED EPITHELIAL MESENCHYMAL TRANSITION

AL. Degryse, H. Tanjore, C. Xu, VV. Polosukhin, TS. Blackwell, WE. Lawson *Vanderbilt University, Nashville, TN.*

Purpose of Study: Current hypotheses suggest that chronic or repetitive lung injury is involved in the pathogenesis of idiopathic pulmonary fibrosis (IPF). Single dose intratracheal (IT) bleomycin is used extensively to induce experimental lung fibrosis. However, the fibrosis is transient and does not recapitulate the histologic features of usual interstitial pneumonia (UIP). Our goal was to develop a recurrent lung injury model using repetitive IT bleomycin that resulted in prominent type II alveolar epithelial cell (AEC) hyperplasia as in UIP.

Methods Used: Mice expressing Cre recombinase under the surfactant protein C promoter (SPC-Cre) were mated to R26Rosa-Stop-LacZ mice that have a loxP flanked STOP cassette upstream of lacZ. Here, Cre irreversibly activates β -galactosidase (β gal) expression in SPC+ epithelial cells, yielding a lung epithelium cell fate reporter system. Wild type C57BL/6J and cell fate reporter mice received IT bleomycin 0.04 units every other week for 8 doses. Mice were harvested at baseline, 2 weeks after a single dose, and 2 weeks after the last repetitive dose. Bronchoalveolar lavage (BAL), frozen tissue, and paraffin embedded tissue were collected.

Summary of Results: Compared to single dose, lungs of mice from the repetitive model had greater AEC apoptosis by TUNEL, less inflammatory cell influx by cell count on BAL fluid, and greater fibrosis. In the repetitive model, type II AEC hyperplasia was prominent, with many cells not only expressing pro-SPC, but also Clara Cell 10 (CC-10), suggestive of a bronchoalveolar stem cell (BASC) like population. Dual immunofluorescence for β gal and fibroblast markers S100A4 and vimentin, indicating fibroblasts derived via epithelial-mesenchymal transition (EMT), was more prominent in the repetitive model. Finally, even 10 weeks after the last repetitive bleomycin dose, lung fibrosis with hyperplastic AECs persisted.

Conclusions: Recurrent IT bleomycin results in marked lung fibrosis with prominent AEC hyperplasia, a pattern that persists well after the last dose of bleomycin. Taken together, this pattern is reminiscent of human forms of lung fibrosis, including IPF.

Southern Society for Pediatric Research

Plenary Session

Young Investigator Award Finalists

8:00 AM

Friday, February 26, 2010

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MULTIVARIATE ANALYSIS OF THE RISK FACTORS FOR MORTALITY AND INTESTINAL FAILURE IN SURGICAL NECROTIZING ENTEROCOLITIS

J. Kelleher¹, TD. Soltan¹, RA. Dimmitt¹, R. Schelonka³, CM. Harmon² ¹University of Alabama, Birmingham, Alabama, Birmingham, AL; ²University of Alabama, Birmingham, Alabama, Birmingham, AL and ³Doernbecher Neonatal Care Center, Oregon Health & Science University, Portland, OR.

Purpose of Study: Univariate comparisons of primary peritoneal drainage (PPD) and laparotomy for mortality and morbidity following surgical

necrotizing enterocolitis (NEC) have been inconclusive. Classification and Regression Tree (CART) analysis allows novel multivariate analyses of risk factors. We hypothesized that PPD is associated with increased mortality or intestinal failure (IF) as defined by discharge home on parenteral nutrition.

Methods Used: Clinical data from infants treated for surgical NEC from 1998–2008 were collected in a retrospective observational study. The population comprised all infants admitted to the neonatal intensive care unit at the Children's Hospital of Alabama who had a surgical procedure for clinically suspected NEC. Univariate and CART analyses were performed to determine risk factors for mortality (death prior to discharge) and intestinal failure (home parenteral nutrition), significance being $p < 0.05$.

Summary of Results: PPD was used in 128 patients and laparotomy in 119. As expected, PPD was associated with greater mortality than those receiving laparotomy (59% vs. 34%). CART analysis revealed that infants with a birth weight > 966 g had greater mortality (71% vs 48% $p < 0.001$) than smaller infants who were treated with PPD. In the PPD subgroup ≤ 966 g, babies with a birth weight ≤ 630 g had greater mortality. For those patients receiving primary laparotomy, infants with a birth weight ≤ 845 g had greater mortality (55% vs 32% $p = 0.01$). Within this subgroup, a laparotomy later than 9.5 days from diagnosis of NEC was also associated with greater mortality (64% vs 33% $p = 0.03$). The type of operation did not predict IF but a birth weight > 1.9 kg was associated with higher IF regardless of operative choice (38% vs 9% $p < 0.001$).

Conclusions: A bimodal birth weight distribution was associated with mortality in the PPD group. A greater birth weight was associated with survival in the primary laparotomy group but also intestinal failure. These data are hypothesis generating for additional risk factors and outcomes in future clinical trials of surgical NEC.

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IMPROVING COUNSELING AT THE THRESHOLD OF VIABILITY WITH VISUAL AIDES

V. Kakkilaya¹, L. Groom², D. Platt¹, L. Conrad², C. Schwab¹, D. Kurepa¹, A. Pramanik¹, G. Caldito¹, T. Davis¹ ¹Louisiana State University Health Sciences Center, Shreveport, Shreveport, LA and ²LSU Health Sciences Center, Shreveport, LA.

Purpose of Study: Neonatologists are regularly involved in counseling pregnant mothers at the threshold of viability. Purpose of our study is to improve the counseling using visual aides (VA).

Methods Used: Pregnant women > 28 weeks gestation attending prenatal clinic were randomly assigned to counseling with or without VA. All were counseled by a single neonatology fellow and received the same information. Women assigned to the VA group were counseled using foam boards containing pictures, graphics, and short messages. The clinical scenario of premature delivery at a gestational age of 23 weeks was presented. Responses to pre counseling questionnaire about the chances of survival, chances of disability and attitudes towards resuscitation were recorded. Information provided during the counseling session included survival rates, morbidity, long term disability, and expected neonatal course. Information regarding the delivery room management with the option of comfort care discussed. A post-counseling questionnaire assessed the ability to recall the information and attitude towards resuscitation.

Summary of Results: In both groups ($n = 69$), the average score for mothers' perception of premature baby's chances for survival were lower after counseling. Women counseled with VA ($n = 36$) had a larger average decrease in score. Women in the VA group were also able to recall a greater number of disabilities ($p = 0.02$) and were significantly more likely to understand the need long term neonatal intensive care unit stay ($p = 0.047$). In both groups, most women were religious and preferred full resuscitation for the premature baby. After counseling, there was a significant decrease in mothers' perception of chance for survival ($p = 0.04$) and a significant increase in the proportion of women who would consider the premature baby will be disabled ($p < 0.01$).

Conclusions: Our study shows that the VA could be a useful tool in perinatal counseling at the threshold of viability. Overwhelming majority of the women opted for full resuscitation. Attitude towards resuscitation did not change despite having a better perception of long term disability in those who received counseling with VA.

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EFFECT OF REVISED IOM WEIGHT GAIN GUIDELINES ON FETAL GROWTH

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Purpose of Study: Women with a BMI of 25 kg/m² are considered overweight by the 2009 revised guidelines and are, therefore, advised to gain 15–25 pounds rather than 25–35 as recommended in 1990. We set out to determine the odds of small and large for gestational age births in light of the original and revised IOM weight gain guidelines.

Methods Used: This retrospective cohort study utilized birth records linked to hospital discharge data for all term, singleton infants > 37 weeks gestation born to Missouri residents (1993–1999) with a BMI of 25 kg/m². We excluded infants born with congenital anomalies or born to mothers with diabetes or hypertension. We completed multiple logistic regression models adjusted for prenatal care, parity, age, education, Medicaid, smoking, and infant gender. Maternal weight gain was classified based on IOM guidelines published in 1990 and revised in 2009.

Summary of Results: The cohort included 14,306 women with a BMI of 25 kg/m² who gained between 15 and 35 lbs. 4712 women (33%) gained 15–25 lbs, 3.1% delivered infants in the lower 3rd percentile for birth weight and 1.3% in the upper 3rd percentile for birth weight. 9594 women (67%) gained 25–35 lbs, 2.4% delivered infants in the lower 3rd percentile for birth weight and 2.7% delivered infants in the upper 3rd percentile. The adjusted odds ratios of being born in the lower and upper percentiles are presented in the Table.

Conclusions: Limiting weight gain in women with a BMI of 25 kg/m², per the 2009 guidelines, increases the risk of low fetal growth but decreased the risk of excessive fetal growth. Further studies should explore the optimal weight gain to reduce the associated outcomes.

	Lower 3rd percentile	Upper 3rd percentile
	aOR (95% CI)	aOR (95% CI)
15-25 lbs weight gain	1.28 (1.03, 1.60)	0.48 (0.36, 0.64)
25-35 lbs weight gain	referent	referent

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SHORT-TERM WEIGHT GAIN AND FEEDING TOLERANCE OF POWDERED VERSUS LIQUID HUMAN MILK FORTIFIER: A BLINDED, RANDOMIZED, CONTROLLED TRIAL

J. Lewis¹, B. Bright², A. Willeitner¹ ¹University of Oklahoma, Oklahoma City, OK and ²University of Oklahoma, Oklahoma City, OK.

Purpose of Study: Human milk is the preferred nutrition for all newborn infants. Benefits of feeding human milk over formula include better neurodevelopmental outcomes, immune protection and prevention of gastrointestinal disease. For small preterm infants, the addition of Human Milk Fortifier (HMF) is necessary to meet their nutritional requirements. Most HMFs are cow-milk based formula products that come in a highly concentrated powdered form (PHMF) or in a less concentrated liquid form (LHMF). Potential advantages of LHMF are better tolerance and increased safety; potential drawbacks include decreased intake of human milk and higher cost. While HMFs are routinely used in NICUs worldwide, there has been little information published comparing LHMF vs. PHMF side by side in a clinical study.

Methods Used: Very low birth weight (VLBW, 500g to 1499g) neonates without major congenital anomalies or gastrointestinal disease admitted to the 88-bed level IV NICU of the University of Oklahoma Health Sciences Center, after informed consent, were randomized to receive LHMF or PHMF (both 24kcal/oz). Infants were monitored for a minimum of 1 week, starting on the first day of fortification. Primary outcome was weight gain (g/kg/d); secondary outcomes included feeding intolerance in terms of residuals (percent of daily intake). The infants' clinical care team and study personnel involved in all documentation and processing of the study data were blinded to the intervention.

Summary of Results: Thirty-eight babies have completed the study period out of a projected 70. The groups were similar in terms of median gestation and median birth weight. Median weight gain was 17.70 g/kg/day for LHMF and 18.4 g/kg/day for PHMF (p -value 0.3307). Per patient, the median percent residual was 3% for the LHMF and 2.5% for PHMF (p -value 0.9645).

The LHM group received approximately 40% less human milk than the PHMF group.

Conclusions: Upon interim analysis, no statistically significant difference was demonstrated between fortification methods in terms of daily weight gain or daily residuals. Specifically, we have not observed a trend favoring LHM over PHMF. However, the amount of human milk consumed was, as expected, significantly lower in the LHM group.

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THE ROLE OF TOLL-LIKE RECEPTOR 9 IN AN ANIMAL MODEL OF NECROTIZING ENTEROCOLITIS

PM. Tatum¹, RG. Lorenz², RJ. Bullock², RA. Dimmitt¹ ¹University of Alabama at Birmingham, Birmingham, AL and ²University of Alabama at Birmingham, Birmingham, AL.

Purpose of Study: Clinical trials have demonstrated that administering probiotic bacteria to premature infants can prevent necrotizing enterocolitis (NEC). While the mechanism is this protection is unknown, probiotic bacterial signaling through toll-like receptor 9 (TLR9) prevents experimental colitis. We hypothesized neonatal mice deficient in TLR9 would have greater intestinal injury compared to wild-type (WT) mice in an animal model of NEC.

Methods Used: Two-week-old C57BL/6.WT and C57BL/6.TLR9^{-/-} mice were used in this study. Cohorts of control mice were injected with bromodeoxyuridine (BrdU) prior to harvesting small intestine. Sections of jejunum were stained with monoclonal antibodies against BrdU to determine enterocyte proliferation as well as standard H&E staining for structural histology. RNA was extracted from sections of jejunum to compare baseline inflammatory molecule expression using quantitative PCR (RT-PCR). Separate mice underwent 60 minutes of superior mesenteric arterial ischemia (I) using a surgically placed micro-aneurysm clip followed by 90 minutes of reperfusion (R). Following sacrifice, sections of jejunum were stained with H&E for assessment of injury as well as apoptosis using TUNEL and activated caspase-3 staining. RT-PCR was used to quantify the inflammatory molecules following I/R injury. Parametric and non-parametric analyses were used where appropriate with p<0.05 considered significant.

Summary of Results: At baseline, TLR9^{-/-} mice had significantly fewer BrdU+ crypt cells and shorter intestinal crypts. When normalized to 18s expression and compared to WT expression, the TLR9^{-/-} intestine had greater baseline amounts of IL-6, myeloperoxidase, and the chemokine KC. Following I/R, the TLR9^{-/-} neonatal mice had significantly greater intestinal injury and apoptosis with increased expression of interferon- γ (IFN- γ) and tumor necrosis factor- α (TNF- α) as determined by RT-PCR.

Conclusions: TLR9 signaling is necessary for early postnatal intestinal development and is protective against a neonatal animal model of NEC. Further studies are needed to determine the role of TLR9 and examine potential clinical applications of its ligand CpG in the prevention of NEC.

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PULMONARY CYTOCHROME P450(CYP)1A1 ENZYME PLAYS A KEY ROLE IN THE ATTENUATION OF HYPEROXIA INDUCED LUNG INJURY IN OMEPRAZOLE-TREATED MICE

B. Shivanna^{1,2}, W. Jiang¹, L. Wang¹, X. Couroucl^{1,2}, B. Moorthy^{1,2} ¹Baylor College of Medicine, Houston, TX and ²Texas Children's Hospital, Houston, TX.

Purpose of Study: Hyperoxia contributes to lung injury in experimental animals and bronchopulmonary dysplasia (BPD) in preterm infants. CYP1A enzymes have been shown to attenuate hyperoxic lung injury in rodents by metabolizing lipid hydroperoxides and peroxides generated by reactive oxygen species. Omeprazole, a proton pump inhibitor used in the treatment of gastric acid related intestinal disorders in humans, induces hepatic CYP1A in vitro. Whether omeprazole induces pulmonary CYP1A1 in vivo is unknown. We hypothesized that omeprazole will attenuate hyperoxic lung injury in adult wild type mice C57BL/6J (WT) by inducing pulmonary CYP1A1 enzyme.

Methods Used: We administered adult WT, Cyp1a1 (-/-), and Cyp1a2 (-/-) mice, i.p., with omeprazole (50 mg/kg, n=14/genotype) or corn oil (CO) (control, n=14/genotype), once daily for 5 days and exposed them to room air or hyperoxia (FiO₂ >0.95) for 72 hours. We estimated lung injury by lung weight/body weight (LW/BW) ratio, histopathology and immunohisto-

chemistry for neutrophils. Pulmonary CYP1A1 expression was determined by enzyme (ethoxyresorufin O-deethylase assay) activities, apoprotein contents (Western blotting with densitometry), immunohistochemistry and mRNA levels (real time RT-PCR).

Summary of Results: Omeprazole decreased perivascular edema, alveolar edema/hemorrhage, neutrophil infiltration, and LW/BW ratio (p<0.001) compared to CO controls in WT as well as Cyp1a2 (-/-) mice exposed to hyperoxia. Attenuation of lung injury paralleled enhanced pulmonary CYP1A1 expression by omeprazole compared to CO controls in WT and Cyp1a2 (-/-) mice. Omeprazole did not protect against oxygen injury in Cyp1a1 (-/-) mice.

Conclusions: Our results provide evidence that omeprazole attenuates hyperoxic lung injury in mice by inducing pulmonary CYP1A1 enzyme. The protective effects of omeprazole may be mediated by CYP1A1 catalyzed detoxification of lipid hydroperoxides. Omeprazole is a potential candidate for clinical trials in the prevention and treatment of BPD in preterm infants.

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IL-10 SIGNALING IS DEVELOPMENTAL REGULATED AND SENSITIVE TO LACTOBACILLUS RHAMNOSIS (LGG) IN DEVELOPING MURINE COLON

J. Mirduri, PW. Lin, NA. Louis Emory University, Atlanta, GA.

Purpose of Study: Necrotizing enterocolitis (NEC) is a devastating inflammatory condition of the premature intestine. IL-10^{-/-} mice show increased vulnerability to experimental NEC, and defects in either IL-10 or the RB subunit of the IL-10 receptor result in commensal-dependent, spontaneous colitis. We have shown that IL-10-mediated inflammatory resolution is dependent on interferon alpha-A (IFN α A) in adult models of colitis, and that commensal flora induce colonic IFN α A in 2 week-old mice. Little is known about the influence of colonization on the expression of IL-10 or its receptor in developing intestine. We hypothesize that IL-10 signaling is critical for regulating inflammation during intestinal colonization, and that probiotic LGG exerts protective effects through IL-10 signaling.

Methods Used: The baseline colonic expression of IFN α A, IL-10, and the IL-10RA, IL-10RB subunits of the IL-10 receptor, was profiled by real-time PCR in 1, 2, 3 week-old, and adult mice. 2 week-old mice were gavaged probiotic LGG or treated with IFN α A by IP injection, sacrificed and analyzed for colonic cytokine and receptor mRNA expression.

Summary of Results: IL-10 expression increased gradually during the first 3 weeks of life and peaking at 3 weeks, while expression of the IL10 receptor peaked at 2 weeks of age, then declined again by 3 weeks. Compared to adults, 2 week-old mice have a 5-fold decrease in IL-10 and 6-fold decrease in IL-10RB mRNA expression. LGG significantly induced IFN α A colonic expression in 2 week-old mice. While neither LGG nor IP injection of IFN α A altered IL-10 expression, both significantly induced colonic expression of the IL-10RB receptor in 2 week-old mice.

Conclusions: Two distinct mechanisms appear to regulate IL-10 signaling with early IL-10 receptor regulation providing a mechanism for increased cytokine sensitivity prior to increases in endogenous cytokine expression. IL-10 is present in breast milk and compensates for deficient IL-10 cytokine production, preventing commensal-dependent colitis in IL-10^{-/-} mice. Thus exogenous IL-10 may be protective in the setting of IL-10 receptor induction early in developing intestine. Furthermore, LGG induces both IFN α A and IL-10RB mRNA in 2 week-old murine colon suggesting a mechanism by which probiotic bacteria regulate inflammation prior to induction of an IL-10 cytokine response.

Cardiovascular Club II - Young Clinician Scientist Award Competition

11:00 AM

Friday, February 26, 2010

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C-REACTIVE PROTEIN MEDIATED VASCULAR INJURY REQUIRES COMPLEMENT

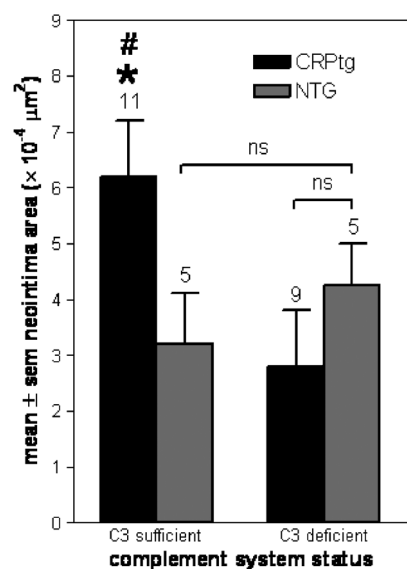
FG. Hage^{1,2}, S. Oparil¹, D. Xing¹, Y. Chen¹, M. McCrory¹, AJ. Szalai¹ ¹University of Alabama at Birmingham, Birmingham, AL and ²Birmingham Veterans Affairs Medical Center, Birmingham, AL.

Purpose of Study: We previously demonstrated that neointima formation in response to vascular injury is exaggerated in human C-reactive protein transgenic (CRPtg) compared to non-transgenic (NTG) mice. We now test the hypothesis that complement is required for this effect.

Methods Used: CRPtg and NTG and their counterparts lacking expression of complement component C3 (CRPtg/C3^{-/-} and C3^{-/-}, respectively) underwent carotid artery ligation. Twenty-eight days after injury mice were euthanized and neointima formation was examined using computer-assisted morphometric analysis of digitized images.

Summary of Results: Neointimal areas were greater in CRPtg vs. NTG (Figure), and this was associated with increased immunoreactive C3 in the lesion and a reduction in serum C3 in CRPtg. In the absence of C3 expression no increase in neointimal area was seen in CRPtg/C3^{-/-} vs. NTG/C3^{-/-} (Figure). For CRPtg, decreasing human CRP blood levels via administration of a selective antisense oligonucleotide eliminated the depletion of serum C3 associated with vascular injury and reduced the deposition of C3 in the lesion. In vitro, human CRP elicited 8-fold increased expression of C3 by bone-marrow derived macrophages from CRPtg and NTG.

Conclusions: Human CRP exaggerates neointima formation in the injured mouse carotid artery, and this is associated with a decrease in circulating C3 and an increase in local deposition of C3.



*P<0.05 vs. NTG/C3 sufficient mice
#P<0.05 vs. CRPtg/C3 deficient mice
ns = not significant

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TREATMENT OF PROSTHETIC VALVE THROMBOSIS: RATIONALE FOR A PROSPECTIVE RANDOMIZED CLINICAL TRIAL

C. Cevik, C. Izgi, W. Dechyapirom, K. Nugent *Texas Tech University Health Sciences Center at Lubbock, Lubbock, TX.*

Purpose of Study: Patients with mechanical heart valves have a life-long increased risk of morbidity and mortality secondary to prosthetic valve thrombosis even though they are on adequate anticoagulation. The European Society of Cardiology, ACC/AHA, and Society of Heart Valve Disease Working Group recommendations have significant disparities. The guidelines lack Class I recommendations and leave the decision to the clinician's experience in most cases. Therefore, optimal treatment of prosthetic valve thrombosis is controversial, and there are no randomized clinical trials available to direct decision making.

Methods Used: We reviewed the original studies, case reports, guidelines, and expert opinions on the management of prosthetic valve thrombosis and

make treatment recommendations for obstructive and nonobstructive thrombotic cases based on the results of the recent reports.

Summary of Results: Although surgical therapy has been the traditional therapeutic approach, recent studies with low-dose and slow-infusion rate of thrombolytic agents have revealed excellent results in these patients. Thrombolysis was superior to surgery in mortality with a success rate of over 80% in most of the studies. Surgery should be considered first in patients with left atrial thrombus, active bleeding, and within the first four days following valve replacement. Patients with non-obstructive prosthetic valve thrombosis can initially be managed with intensification of anticoagulation if the thrombus diameter is less than 5 mm.

Conclusions: Our literature review demonstrated the mortality benefit of thrombolytic therapy compared to surgery in patients with thrombotic mechanical heart valves. Therefore, thrombolytic therapy should be considered more often in the treatment of these patients. Management of prosthetic valve thrombosis is still controversial. Obviously, a prospective randomized clinical trial is needed, and this can be achieved by developing an international database for patient enrollment and randomization into available treatment strategies.

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OXIDATIVE STRESS, MITOCHONDRIAL PERMEABILITY TRANSITION PORE OPENING AND CARDIAC HYPERTROPHY WITH FIBROSIS IN ALDOSTERONISM: RESPONSE TO SUPPLEMENTAL ZINC

G. Kamalov, R.A. Ahokas, W. Zhao, AU. Shahbaz, SK. Bhattacharya, Y. Sun, IC. Gerling, KT. Weber *University of Tennessee Health Science Center, Memphis, TN.*

Purpose of Study: Aldosterone/salt treatment (ALDOST) leads to secondary hyperparathyroidism (SHPT) with parathyroid hormone-mediated intracellular Ca²⁺ overloading and the induction of oxidative stress in cardiomyocytes and mitochondria with opening of the mitochondrial permeability transition pore (mPTP), which eventuates in necrosis with subsequent scarring. Concomitantly, Zn²⁺-based antioxidant defenses are reduced. We hypothesized a Zn²⁺ supplement would ameliorate the prooxidant:antioxidant imbalance and prove cardioprotective.

Methods Used: Eight-wk-old uninephrectomized rats received 4 wk ALDOST alone or with ZnSO₄ cotreatment (40 mg/day; gavage) and were compared to unoperated/untreated age-/sex-matched controls (n=6/group). We monitored: arterial pressure; echocardiographic ventricular function; fibrosis by histochemistry; cardiomyocyte size by planimetry and hypertrophy by myosin heavy-chain (MHC-α and -β) and pro-atrial natriuretic peptide (ANP) mRNAs; biomarkers of oxidative stress, including mitochondrial H₂O₂ production; mPTP opening; and endoplasmic reticulum (ER) stress by BiP/GRP78 and protein disulfide isomerase (PDI) using RT-PCR and immunoblotting.

Summary of Results: Compared to ALDOST alone, ZnSO₄ cotreatment: attenuated (p<0.05) scarring and the rise in collagen volume fraction (4.79±0.87 and 3.89±0.34%, respectively, vs. controls 2.22±0.04%); improved depressed (p<0.05) fractional shortening seen with ALDOST (53±2 vs. 42±5% and controls 46±2%), without preventing hypertension or compensatory hypertrophy; reduced (p<0.05) oxidative stress, including mitochondrial H₂O₂ production and ER stress while preventing mPTP opening. Furthermore, ZnSO₄ cotreatment attenuated upregulation of MHC-β, a marker of pathologic hypertrophy.

Conclusions: In the hypertrophy that accompanies the SHPT of aldosteronism, the induction of oxidative stress, coupled with mPTP opening, ER stress and reduced antioxidant defenses, contribute to cardiomyocyte necrosis and scarring with reduced shortening. This prooxidant phenotype can be overcome by fortifying the heart's antioxidant capacity with a Zn²⁺ supplement.

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INFUENCES OF ALPHA AND BETA ADRENERGIC GENE VARIATION ON LEFT VENTRICULAR DIASTOLIC FUNCTION IN THE JACKSON COHORT OF GENOA

C. Drago, A. Penman, S. Musani, T. Mosley, E. Fox *UMMC, Jackson, MS.*

Purpose of Study: Diastolic function, defined by the mitral diastolic early (E) and late (A) inflow velocities, is related to hypertension and prognostic for mortality in African Americans. The potential influence of genes in the adrenergic pathway on left ventricular (LV) diastolic function has not been sufficiently studied in this high-risk group. We assessed the relation of genetic variation to LV diastolic function in a cohort of hypertensive African American siblings from the GENOA study using single nucleotide polymorphisms (SNPs) in nine diallelic candidate genes in the alpha and beta adrenergic pathway.

Methods Used: Hypertensive probands were ascertained if they were in a sibship with ≥ 2 individuals with essential hypertension diagnosed prior to age 60. Covariate-adjusted linear regression residuals were regressed on each genotype in a generalized estimating equations additive model for mitral A wave velocity and mitral E wave velocity. Men and women were analyzed separately.

Summary of Results: The study population consisted of 1,381 participants representing approximately 550 sibships (72.1% women, mean age 62.8 ± 9.4). The mean ($\pm$ standard deviation) for the mitral A and E wave velocities was 64.0 ± 18.2 and 67.5 ± 17.2 in men and 71.9 ± 19.2 and 73.9 ± 18.4 in women, respectively. We found the *h2807* in the alpha adrenergic B2 receptor gene (*ADRA2B*) was significantly associated with early diastolic filling velocity in women. ($p=0.00069$).

Conclusions: In this cohort of hypertensive African American siblings, we identified a SNP in *ADRA2B* on chromosome 2 that shows significant association with mitral E diastolic filling velocity in women.

Adolescent Medicine and Pediatrics

Concurrent Session

2:00 PM

Friday, February 26, 2010

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HPV VACCINATION AND ACCEPTANCE AMONG INNER CITY PREADOLESCENT AND ADOLESCENT FEMALES

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Purpose of Study: In the US alone, six million HPV infections occur each year. Few adolescents and young women believe that the HPV vaccine is protective. Despite a moderate uptake of the vaccine, many females at risk of acquiring HPV have not yet received the vaccine. The vaccine is approved for females ages nine years and older and recommended for age eleven and older. The objective of our study was to evaluate HPV vaccine acceptance and compliance among indigent preadolescent and adolescent females.

Methods Used: Between September and November of 2008, medical records of 9 to 17 year old females attending an inner-city university affiliated clinic were reviewed. Demographic data, HPV immunization status, missed opportunity and vaccine refusals were recorded and analyzed using chi-square method.

Summary of Results: Racial distribution (82% African American, 11.5% Caucasian, 6% Hispanic) was proportionate to clinic population. Of 1,108 age-eligible females, 897 were offered the vaccine: 69% (766 of 897) accepted/received the vaccine, 6% (105 of 897) refused. Opportunities to offer the vaccine were missed overall in 19% (211 of 897). Children in the nine and ten year old age group were more likely to have missed opportunities (44%) and less likely to have received at least one vaccine dose ($p<0.0001$). In 11 to 17 year olds, as the child gets older the more likely they are to receive vaccine ($p=0.033$). No difference was noted in vaccine refusal by age ($p=0.111$) nor in vaccine outcome by race ($p=0.181$). Thirty-seven percent of 11 to 17 year old vaccine recipients completed the series or were current compared to 20.5% of the 9 to 10 year olds.

Conclusions: The high number of missed opportunities point to the need for vigilance in offering the vaccine. With their knowledge of the HPV vaccine, primary care physicians play an important role in vaccine acceptance, particularly in the younger age eligible females where higher protection has been reported the earlier the vaccine is received. Beyond setting appointments for subsequent doses, additional steps need to be undertaken to improve the completion of the vaccine series.

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ASSOCIATIONS WITH ADOLESCENT IMMUNIZATION

P. Dasari, L. McGuinn, PM. Darden *University of Oklahoma Health Sciences Center, Oklahoma City, OK*

Purpose of Study: While the predictors of childhood immunization are well studied. Much less is known about those predictors for adolescents. What factors are associated with changes in adolescent vaccinations and is it similar across different vaccines.

Methods Used: Adolescents aged 12 to 17 years in the 2007 National Survey of Children's Health (NSCH) were analyzed. NSCH is a national complex sampling design telephone survey of parents designed to allow state and national inferences. Up to date (UTD) is the receipt of a Td/Tdap since 11 yrs, MCV4 and, for girls, any HPV. We also examined UTD not including HPV (UTDb). Analyses were appropriate to the complex study design. Unless otherwise noted all comparisons are statistically significant.

Summary of Results: Overall, 20% were UTD. Without HPV, UTDb was 32%. Tdap vaccination was 83% and varied by age, from 66% at 12 to 90% at 17 years. MCV4 was 39% and HPV was 18% (girls only) neither varied by age. Immunization rates for all vaccines as well as UTDb were consistently lower for girls vs. boys (Tdap, 82% vs 84%; MCV4 38% vs 40%; UTDb 32% vs. 33% all $P=NS$). For girls whose doctor recommended HPV had the highest immunization rates than those who did not; Tdap 91% vs. 77%, MCV4 52% vs. 30%, HPV 49% vs 4%. UTD was not associated with health insurance, maternal education or having a usual doctor. However, UTDb vaccination rates were highest at 39% (vs 31% for HS and 33% for >HS, $p=0.02$) in adolescents with mothers who did not complete high school.

Conclusions: Each vaccine in adolescent has different acceptance rates for reasons that are not completely clear. Clinicians who recommend vaccines make a tremendous difference in adolescence immunization rates.

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THE CONTRIBUTION OF POSTPARTUM PSYCHOSOCIAL VARIABLES TO INFANT LENGTH OF STAY IN THE NEONATAL INTENSIVE CARE UNIT

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Purpose of Study: The purpose of the present study was to assess psychosocial variables in mothers of neonates admitted to the NICU and assess the contribution of related psychosocial variables to neonate length of stay (LOS) in the NICU. Our central tenet was that poor maternal psychological functioning would be associated with increased neonate LOS in the NICU.

Methods Used: Mothers of NICU infants with congenital anomalies, who required surgery, who had significant cardiac abnormalities, or who had chromosomal defects were excluded from participating. Eligible participants were initially identified by the project coordinator upon the infant's admission to the NICU. PPD, postpartum social support, postpartum NICU stress, and maternal anxiety were assessed at two weeks postpartum.

Summary of Results: There were a total of 111 participants. The diagnosis or treatment of a disorder prior to the pregnancy was reported to be 25.2% for depression, 22.7 % for anxiety, and 7.2% for a substance use disorder and during the pregnancy was reported to be 10.8% for depression and 6.3% for anxiety. The majority of women (52.3%) received a positive screening for major postpartum depression and an additional 29.7% received a score indicating that they were "at-risk." The mean score for trait anxiety on the STAI was 40.33 (SD=9.88), which was significantly higher than the published norms. Length of stay in the NICU was significantly correlated with trait anxiety ($r=.227$), as well as stress associated with the NICU environment including infant appearance ($r=.321$) and changes in parental role that differ for parents of sick infants ($r=.201$).

Conclusions: The majority of participants had a positive screening for post partum depression, anxiety, and stress related to the NICU environment. The

significant correlations of trait anxiety as well as stressors associated with the physical appearance of the infant and parental role with length of stay in the NICU support the tenet that postpartum psychological functioning is related to length of stay for infants in the NICU.

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VALIDITY OF SUBJECTIVE SCORING ON THE AUTISM DIAGNOSTIC OBSERVATION SCHEDULE

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University of South Alabama, Mobile, AL.

Purpose of Study: The Autism Diagnostic Observation Schedule (ADOS) is a semi-structured standardized assessment that is widely used in the evaluation of children suspected of having autism spectrum disorders. The present study tests the validity of subjectively scored observations during the ADOS.

Methods Used: DVD recordings of 60 Module 1 ADOS evaluations were reviewed by an observer blind to clinical history and final diagnosis. Behaviors that could be quantified (i.e., response to name, pointing, showing, requesting, echolalia, and repetitive movements) were compared with their corresponding subjective ADOS subtest scores. Pearson's chi-square and t-tests were used for data analysis.

Summary of Results: Response to name, pointing, and requests were each highly correlated with ADOS scores ($p < 0.001$), although these items do not load into the ADOS scoring algorithm. Showing, echolalia, and repetitive behaviors showed non-significant correlations in the expected directions. Scores of showing, eye contact, and shared enjoyment did not differ based on child attractiveness ratings. Highly significant differences between Autism Spectrum Disorder (ASD) and non-ASD groups were found in response to name, requests, and specific gestures. Surprisingly, neither echolalia nor repetitive movements distinguished between the ASD and non-ASD groups.

Conclusions: Subjective scoring of the ADOS is validated by objective tallies of discrete behaviors by an independent observer. Highly significant differences on a number of specific behaviors were found between the ASD and non-ASD groups, supporting the use of the ADOS to assist with clinical diagnosis.

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ABNORMAL DEVELOPMENTAL SCREENS AND PATIENT CHARACTERISTICS

L. McGuinn, PM. Darden *University of Oklahoma Health Sciences Center, Oklahoma City, OK.*

Purpose of Study: Guidelines advocate use of standardized developmental screens in pediatric offices. The rate of abnormal results expected is unknown. The purpose of this study is to determine 1) the prevalence of positive screens in a sample of US children, 2) the proportion of children who screen positive and are not identified as Children with Special Health Care Needs-CSHN.

Methods Used: Children age 4 mo-5 yrs in the 2007 National Survey of Children's Health-NSCH were analyzed. NSCH is a telephone survey with complex sampling design to allow state and national inferences. Results classified as high and moderate risk on the Parents' Evaluation of Developmental Status-PEDS (contained in the survey) were considered as positive, low or no risk as negative. CSHN were identified by a validated questionnaire. Analyses accounted for the complex study design. Unless noted, all comparisons were statistically significant.

Summary of Results: The prevalence of positive PEDS was 26%, varying from 12% at 4-5 mo to 38% at 5 yr ($P < 0.1$). CSHN were 12%, with 2% at 4-5 mo to 17% at 5 yr. Children with positive PEDS were more likely CSHN (45% v. 24%). Having a positive PEDS was associated with female gender (29% v. 23%), public v. private insurance (33% v. 22%), no usual provider of care (33% v. 26%) and maternal education ($< HS$, 35%, HS 29%, $> HS$ 23%). A positive PEDS was not associated with a Dr. asking about development or a parent-completed developmental screen. CSHN were more likely to be identified if asked about development (13% v. 11%), to have received a

parent completed screen (12% v. 11%) or both (19% v. 11%). 79% of those with positive PEDS were not identified as CSHN. PEDS positive and not CSHN was associated with age, varying from 97% at 4-5 months to 78% at 5 years, lack of usual Dr., 88% v. 78%, not using a developmental questionnaire and Dr. asking about development, 84% v. 63%. In multivariate analysis, independent predictors of being PEDS positive while not being id as a CSHN included age, gender, insurance, and having a Dr. use a formal screen. Maternal education and having a usual doctor were not significant.

Conclusions: This study determined prevalence rates of abnormal developmental screening by age in children. Asking about development together with using a structured tool resulted in fewer missed children at risk for developmental abnormalities.

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DIFFERENCES IN SEPTIC WORK-UPS IN THE EMERGENCY DEPARTMENT FOR FEBRILE INFANTS LESS THAN 3 MONTHS DURING INFLUENZA AND RSV SEASON

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Purpose of Study: Febrile neonates less than 31 days of age presenting to the Emergency Department (ED), without source, undergo a full septic work-up (blood, urine and spinal fluid cultures) for the presence of occult bacterial infection. These guidelines are generally followed in infants less than 3 months. Additionally, winter months are challenging with large numbers of febrile infants in the ED. Recent studies seek to identify infants at low risk who could tolerate abbreviated septic work-ups. We sought to determine if septic work-ups differed among neonates and older infants during the Influenza or Respiratory Syncytial Virus (RSV) season at Arkansas Children's Hospital (ACH), and if any bacterial infections were discovered post admission.

Methods Used: Chart review identified 237 infants less than 3 months of age who were seen and admitted through the ED from 7/31/05 to 6/30/08. Comparisons of septic work-ups done during In (influenza and RSV) and Off season as well as differences between neonates and older infants 31-to 89 days were performed. Bacterial infections found via additional work-up obtained on the floor were also examined.

Summary of Results: Neonates (less than 31 days) comprised 91.1% of identified patients and were more likely to receive a full septic work-up than older infants (70.7% vs. 29.6%, $p < 0.001$). Patients were less likely to receive a full septic work-up if they tested positive for either influenza or RSV (33.3% vs. 71.3%, $p < 0.001$), but seasonality itself did not affect work-up (62.8% during In season vs. 71.1% Off season, $p = 0.15$). 24.2% of patients received subsequent work-up after admission, all less than 30 days of age. In 13 cases (4.8%) when patients did not receive a full septic work-up subsequent "missed" bacterial infections were found; 84.6% were bacteremia, 7.6% UTI, and 7.6% salmonella found only in stool. One neonate with RSV was found to have a missed bacterial UTI.

Conclusions: Seasonality did not affect the work-up of infants in the ED, but age and the presence of a positive RSV or Influenza culture did. Most "missed" infections were bacteremia and occurred in neonates who did not receive a full septic work-up upon admission. The presence of bacterial infections coexisting with viral syndromes advocates for continued full septic work-ups in neonates.

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BLOOD PRESSURE SCREENING IN PEDIATRIC PRIMARY CARE SETTINGS

TC. Wall *University of Alabama at Birmingham, Birmingham, AL.*

Purpose of Study: To assess knowledge of pediatric hypertension (HTN) and describe blood pressure (BP) screening and treatment practices among a group of primary care providers in the control arm of a randomized controlled trial (RCT) to improve screening practices in pediatric primary care settings.

Methods Used: Pediatric providers were enrolled in a RCT of a multifaceted intervention to improve screening in primary care settings. State Medicaid claims data from Alabama, South Carolina, and Illinois were used to identify

eligible providers, defined as those that had seen at least 8 children ages 3 or 4 years old for well-child visits over a 12 month period. Both intervention and control arm participants completed internet-based educational modules, with control arm modules focusing on screening and evaluation for HTN. Enrolled providers were randomized at website login. Modules were case-based and contained embedded questions to assess knowledge and practice. BP screening modules provided standardized pediatric BP tables for reference.

Summary of Results: There were 65 respondents in the HTN module. BP measurement techniques were aneroid (42.4%), mercury (30.3%), and oscillometric (27.3%). Only 4 participants could correctly identify criteria for choosing cuff size relative to arm size; 24% reported choosing cuff size based on child's age and 32% based on manufacturer's markings. Age was correctly identified by the majority (96%) as a factor determining normal BP, but only about half identified height and gender as factors. Only 49% reported the incidence of HTN among obese adolescents to be as high as 25–30%. Earliest age for routine BP screening was reported as 3 yrs by 64% (12 months 6%, 2 yrs 9%, 4 yrs 18%, teens 3%). No participants identified prematurity as reason for routine monitoring of BP in infancy. Of 4 cases presented, patients' BPs were correctly classified in 64–80% (normal/borderline/stage 1 HTN/stage 2 HTN). In 2 scenarios of teenagers meeting diagnostic criteria for HTN (at least 3 elevated measurements on 3 different days), only 4 participants would start BP medications.

Conclusions: About 1/5 of participants reported not initiating BP screening by age 3 years. Most participants were able to correctly classify BP severity using tables of standard BP norms. Few participants were comfortable starting BP medications in patients meeting diagnostic criteria for HTN.

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DEVELOPMENT & TESTING OF AN INTERACTIVE WEB-BASED PROGRAM TO FACILITATE READINESS & MOTIVATION FOR SMOKING CESSATION

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Purpose of Study: The purpose of the study was to develop an interactive web-based computer program to facilitate motivation and readiness to engage in smoking cessation, and compare changes in motivation and readiness to engage in smoking cessation after the delivery of an interactive web-based smoking cessation computer program.

Methods Used: Recruited from a general pediatric outpatient clinic, 114 parents (24 fathers) were randomly assigned to either a web-based computer program intervention (CPI) or to receive treatment as usual (TAU). The web-based computer program was based on stages of change and motivational interviewing principles and provided assessment and personalized feedback on parental smoking behavior, parental health risk, and child health risk, and provided smoking cessation resources. Inclusion criteria required that the parent was a current smoker not actively attempting smoking cessation, could read at least at an 8th grade level, and speaks English as their primary language. In addition to demographic information parents also completed measures assessing readiness, importance, confidence, and motivation to stop smoking at baseline. One month following the intervention all parents were contacted to complete the measures again, with 72 parents (13 fathers) doing so.

Summary of Results: Preliminary analyses indicated significant group differences with regard to ethnicity, income, and average number of cigarettes per day at baseline. Therefore, subsequent analyses covaried out these variables. Primary analyses demonstrated a significant association between intervention and stages of change for smoking behavior ($p = .046$), compared to TAU parents, CPI parents increased in their readiness to change their smoking from baseline to 1-month follow-up.

Conclusions: The current study demonstrated the feasibility of developing and implementing an interactive web-based program to facilitate smoking cessation. Furthermore, this intervention was found to be effective at increasing readiness to change parental smoking behavior.

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GLAUCOMA SUSPECT IN CHILDREN: A CHALLENGING ENTITY

M. Harrison, Z. Prasla, MA. Roensch, F. Marquardt, B. Adams-Huet, K. Kooner *UT Southwestern, Dallas, TX.*

Purpose of Study: Glaucoma suspects are patients presenting with one or more of the common risk factors associated with glaucoma, but lack the corresponding visual field deficiencies. Early identification and awareness of such individuals may encourage prompt treatment at the earliest sign of progression and prevent vision loss in the future. Unfortunately, as visual field information is not always available in children, very little information exists about pediatric glaucoma suspects. Our purpose is to determine epidemiological data from 75 pediatric glaucoma suspects in the ethnically diverse North Texas population.

Methods Used: A review of Dallas Glaucoma Registry identified 230 patients with glaucoma at the Children's Medical Center in Dallas TX. 75 were identified as glaucoma suspects. We collected demographic information, values for intraocular pressure (IOP), visual acuity and cup to disk (C/D) ratios. Glaucoma suspect factors were: IOP of ≥ 21 mmHg, suspicious optic disks (SOD), and a strong family history of glaucoma (FHx). Prevalence and severity of risk factors among different ethnic groups were analyzed using SAS v9.2 (SAS Institute, Cary, NC, USA).

Summary of Results: The C/D ratios of African Americans (.73), Hispanics (.68) and Asians/East Indians (.68) were all significantly higher than those of Caucasians (.56). ($P = 0.001$, $P = 0.01$ and $P = .04$ respectively) No statistically significant difference existed between African Americans, Hispanics and Asians/East Indians. The second most common risk factor was elevated IOP, with 33% of the study population presenting with an average IOP of 19.6 ± 5.3 mmHg.

Conclusions: Suspicious optic disks was the most common factor in pediatric suspects. The differences found in C:D ratios between African American and Caucasian suspects are greater than those found in healthy children. Our study shows that race and other ocular risk factors may play a major role in diagnosing glaucoma in children.

[bold] Glaucoma Suspects [bold]	No. of Suspects (% of study population)	Mean C/D Ratio (SD)	Mean IOP (mmHg)
African American	20 (26.7)	.73 (.09) 30 eyes	18.75 (12 eyes)
Caucasian	20 (26.7)	.56 (.14) 18 eyes	21.47 (15 eyes)
Hispanic	28 (37.3)	.68 (.12) 44 eyes	18.19 (13 eyes)
Asian/East Indian	7 (9.3)	.68 (.11) 11 eyes	19.58 (6 eyes)

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PEDIATRIC RESIDENTS AND TEEN DRIVING ISSUES

T. Gibbs, M. Nichols, K. Monroe *Univ of Alabama, Birmingham, AL.*

Purpose of Study: Evaluate pediatric residents' knowledge of teen driving risks, laws, and counseling practices.

Methods Used: An eight question online multiple choice survey of 69 pediatric and combined medicine/pediatric residents. Data gathered via survey monkey.com. Questions asked include residents familiarity with Graduated Drivers License, most common cause of death for teenagers, and barriers to discussing driving with teenage patients.

Summary of Results: Total of 35 responses (approximately 50% of residents) were obtained. The breakdown of residents was 34% interns, 29% second year residents, 29% third year residents and 8% fourth year med/peds residents. All residents knew that the number one cause of death for teenagers is motor vehicle crashes. When asked how often residents counseled teenagers about the dangers of teen driving only 5% counsel at every visit and 31% sometimes at visits. The percentage of residents who rarely or never counseled parents about their teen driving was 73%. In regards to Alabama's Graduated Driver License law 46% had never heard of the law. Barriers that exist in talking to teens about driving include lack of time at visits (71%), lack of physician knowledge (51%) and teenagers won't listen (11%). Over half of residents surveyed (54%) were not comfortable talking with parents and teens about driving laws.

Conclusions: Pediatric residents are not discussing teen driving with parents and teenagers on a consistent basis. Residents are also not aware of the current Graduated Drivers License law for their state. Targeted efforts to increase resident knowledge are much needed.

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TEENAGE DEPRESSION IN A MOBILE PEDIATRIC CLINIC

R. Arnberger, D. Usner, M. Johns, V. O'Connor, A. Olteanu *Tulane University School of Medicine, New Orleans, LA.*

Purpose of Study: The New Orleans Children's Health Project (NOCHP) is a mobile clinics program developed as a partnership between the Children's Health Fund and Tulane School of Medicine. It operates out of two state-of-the-art mobile medical units, according to the enhanced medical home model. One unit offers pediatric primary care and the second unit assists children with mental health services. This integration of pediatric and mental health services allows NOCHP to provide comprehensive preventative and treatment services and facilitates the detection and treatment of mental health disorders, particularly depression. Depression is a severe condition that has been increasingly recognized among adolescents. Previous studies show prevalence of depression among adolescents as high as 20%. Early detection and treatment of major depression at the pediatric level is essential in potentially reduce the occurrence of the chronic illness in adulthood. We discuss how our clinic was successful in implementing an effective depression screening process and we report our results.

Methods Used: NOCHP implemented a depression screening protocol in teenagers ages 11–18 years. The protocol was designed to systematically and consistently screen all patients 11–18 years old for symptoms of depression using the Patient Health Questionnaire-2 (PHQ-2), a two question initial screening for possible depression. For patients with a positive PHQ-2 screening, a Patient Health Questionnaire-9 (PHQ-9) was also administered. All patients who screened positive on the PHQ-9 questionnaire were referred to the mental health unit for depression evaluation and treatment.

Summary of Results: Over a period of 12 months, 107 patients ages 11–18 years were screened for depression. A total of 30 patients (28%) screened positive on the PHQ-9, indicating they were experiencing symptoms consistent with a diagnosis of depression at the time of screening. More than half of the patients were either African-Americans or Hispanics.

Conclusions: Our patients may be experiencing symptoms of depression at a higher rate than the general population. The close collaboration between the mental health and medical team on two mobile units allowed us to implement this depression screening initiative in four underserved communities in the Greater New Orleans area.

Allergy, Immunology, and Rheumatology I

Concurrent Session

2:00 PM

Friday, February 26, 2010

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ABSENCE OF SPHINGOSINE KINASE 1 INHIBITS JOINT EROSIONS IN TNF-ALPHA INDUCED ARTHRITIS

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Purpose of Study: Sphingolipids, constituents of the plasma membrane, can alter cellular functions. Sphingosine 1 phosphate (S1P) in vitro is required for TNF α induced COX-2 and PGE2 production while, stimulation with TNF α and S1P leads to more COX-2 and PGE2 than either alone. Both sphingosine kinase (SphK) 1 and 2 are upregulated in rheumatoid synovium compared to osteoarthritis synovium. Additionally, S1P1R, an S1P receptor, is upregulated in RA patients. Fibroblast-like synoviocytes (FLS) proliferate with proinflammatory cytokines and produce COX-2 and PGE2 with TNF α and S1P. We hypothesized that S1P, induced by TNF α is a critical mediator of inflammation and joint damage in the rheumatoid joint.

Methods Used: The following experiments were performed to test this hypothesis: Transgenic hTNF α mice were crossed with SphK1 $^{-/-}$ mice and genotyped by PCR. Arthritis in these mice develops independent of antigen, T cells or B cells. The mice were observed weekly for disease activity, while CT images and microarray analysis were used to evaluate disease activity in the joint and evaluate genetic profiles respectively.

Summary of Results: hTNF/SphK1 $^{-/-}$ mice (n=15) had significantly decreased clinical joint disease compared to hTNF/SphK1 $^{+/+}$ mice (n=18), with average arthritis scores of 1+/-0.5 vs. 5+/- 1.2 respectively at 5 months (based on joint swelling and deformity). An erosion Index, measured quantitatively from 3D CT images of the ankles was significantly decreased

in hTNF/SphK1 $^{-/-}$ mice at 4 and 5 months, with a 2 fold decrease in erosions in hTNF/SphK1 $^{-/-}$ vs. hTNF/SphK1 $^{+/+}$ mice. Microarray analysis of ankle joint synovium, with RT-PCR confirmation, demonstrated significant modulation of a cluster of genes regulated by SOCS3 in hTNF/SphK1 $^{-/-}$ mice compared to hTNF/SphK1 $^{+/+}$ mice.

Conclusions: Genetic deletion of SphK1 significantly decreased the severity of hTNF α induced arthritis, decreased erosions and led to upregulation of SOCS3 with impact on expression of SOCS3 related genes. These data indicate that S1P plays a key role in TNF α induced joint inflammation and erosions and is a potential target for therapeutic intervention in inflammatory arthritis.

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LUNG DISEASE ASSOCIATION WITH EXTRA-ARTICULAR MANIFESTATIONS OF RHEUMATOID ARTHRITIS

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Purpose of Study: Little information exists about the relationship between lung disease (LD) and extra-articular rheumatoid arthritis (ExRA). We evaluated the association of LD and ExRA manifestations in the Veterans Affairs RA (VARA) registry.

Methods Used: A subpopulation of 579 VARA patients at the Jackson, MS and Dallas, TX VA hospitals were identified for inclusion. Each patient's medical record was abstracted to identify LD (nodules, interstitial lung disease and pleural effusion/pleuritis), and ExRA manifestations: skin, kidney, cardiac, vascular, bone (osteoporosis), ocular, neurologic, hematologic (Felt's, and lymphadenopathy), lymphoma, sicca syndrome and vasculitis. Demographics, disease duration, inflammatory markers, smoking status, CCP and RF were recorded. Statistics included frequency, chi-square and regression analyses to evaluate the correlation of LD with ExRA manifestations.

Summary of Results: The study population was mostly male (89%), Caucasian (78%) and older (mean 64 years). Mean disease duration was 16 years. Overall, 96% of this VARA cadre had a range of 1–8 ExRA manifestations (mean = 4). LD occurred in 25.5% of the population. However, only 2.2% had a LD as their sole manifestation. The majority of LD patients had 3–4 organ systems with ExRA manifestations (58%) and 33% had more than 5 systems involved. LD correlated most strongly with skin nodules (p = 0.004), and cardiac manifestations (p = 0.004) followed by bone (p = 0.005) and hematologic (p = 0.02) involvement. Patients with LD were significantly more likely to be male (95% vs. 87%) and have positive RF and CCP (96% vs. 89% and 83% vs. 75%) compared to those patients with non-LD. RF was associated with LD (p = 0.001). There was no LD association with overall smoking (current and former).

Conclusions: ExRA may be an underappreciated occurrence in older populations or predominantly male subsets. When ExRA is focused on LD there are strong associations with being male, as well as bone, skin and hematological comorbidities. Such findings are more prevalent than previously reported and may represent the uniqueness of the VA's vertical integrated system to be able to capture chronic disease occurrences in elderly males.

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NUCLEAR EXPRESSION OF CXCR5 IN SPLEEN FOLLICULAR T HELPER CELLS IN AUTOIMMUNE BXD2 MICE

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Purpose of Study: CXCR5⁺ follicular T helper (T_{fh}) cells primarily help B cells differentiation into antibody producing plasma cells and memory B cells. Interaction of cell surface CXCR5 with its ligand CXCL13 is an important mechanism to direct the migration of CD4 T and B cells to germinal center (GC) light zone area. The purpose of this study is to determine how CXCR5⁺ T_{fh} cells are involved in the pathogenic GC response in autoimmune BXD2 mice.

Methods Used: Single cell suspensions prepared from the spleens of BXD2 mice and normal B6 mice were subjected to FACS staining with some cells cytopspinned for fluorescent imaging analysis. Frozen spleen sections were used for fluorescent confocal imaging analysis. Paraffin-embedded spleen

sections were used for immunohistochemistry (IHC) staining. Subcellular expression of CXCR5 in purified CD4 T cells was determined by western blot analysis.

Summary of Results: There was 2.5- and 1.5-fold increased expression of ICOS⁺CXCR5⁺ and IL-21⁺ CD4⁺ T cells, respectively, in the spleens of BXD2 compared to that in B6 spleens. ICOS⁺CXCR5⁺ CD4⁺ T cells mainly clustered in GCs and were close to CD21/CD35⁺ follicular dendritic cells, suggesting these are the commonly known T_{fh} cells. CXCR5 was rarely expressed by naive CD4 T cells. Surprisingly, CXCR5⁺ was mainly detected inside the nucleus but not on cell membrane of CD4 T cells in GC light zone. Nuclear expression of CXCR5 on these CD4 T cells was further confirmed by IHC and fluorescent staining. Western blot and FACS imaging analysis both showed that there was increased nuclear expression than cytoplasmic expression of CXCR5 in CD4 T cells from BXD2 mice. Importantly, nuclear CXCR5 co-localized with Ki67 by IHC staining. CXCR5⁺CD4⁺ T cells from BXD2 mice expressed higher levels of BrdU and lower levels of Fas, compared to those from B6 mice. **Conclusions:** There is expansion of T_{fh} cells in autoreactive GCs in BXD2 mice. T_{fh} showed an unexpected nuclear expression pattern of CXCR5. Nuclear translocation of CXCR5 might arrest T_{fh} cells after their migration into the GC light zone. It may further play an important role in increasing proliferation or inhibiting apoptosis of T_{fh} to facilitate the autoreactive GC responses.

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PERIPHERAL NEUROPATHY IN SJÖGREN'S SYNDROME

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Purpose of Study: Sjögren's syndrome is chronic, not uncommon autoimmune disease that primarily affects the salivary and lacrimal glands and is characterized by autoantibodies binding the Ro/La ribonucleoprotein particle as well as lymphocytic infiltrates in affected exocrine glands. Some patients have extraglandular manifestations, which can include a peripheral neuropathy similar to that seen in Vitamin B 12 deficiency. We undertook this study to peripheral neuropathy in a well characterized cohort of Sjögren's syndrome patients.

Methods Used: We evaluated 66 consecutive Sjögren's syndrome patients attending a dry eyes/dry mouth clinic for peripheral neuropathy. Each subject underwent a comprehensive ophthalmological, dental, medical and laboratory examination, including a minor salivary gland biopsy. Anti-Ro and anti-La were determined double immunodiffusion and ELISA. Subjects were classified according to the Combined American-European Sjögren's syndrome classification criteria. Peripheral neuropathy was considered present if vibratory sensation, 10-gram filament sensation or proprioception was abnormal.

Summary of Results: We found that in 24 (36%) of the 66 patients, this neuropathy was present. Neuropathy was related to serology with 6 of 9 (66.6%) of patients with both anti-Ro and anti-La having neuropathy while 18 of 57 (31.5%) of those without anti-Ro/La had neuropathy ($\chi^2=4.135$, $p=0.04$, odds ratio=2.1). When anti-Ro and anti-La were determined by ELISA there was no statistical association to neuropathy. The relationship of neuropathy to other aspects of Sjögren's syndrome such as focus score as well as to level of serum vit 12 is under exploration.

Conclusions: Mild peripheral neuropathy is common among patients with Sjögren's syndrome and is found twice as frequently among those patients with anti-Ro and anti-La when determined by immunodiffusion.

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PREGNANCY IN SYSTEMIC LUPUS ERYTHEMATOSUS: A THREE YEAR RETROSPECTIVE ANALYSIS

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Purpose of Study: Systemic lupus erythematosus is a disease primarily affecting woman of childbearing age. Pregnancy and its clinical manifestations, therefore, are of great concern to the physicians managing both of these conditions. The aim of this study was to compare the outcomes and complications of pregnancy in patients with SLE to see if any correlations could be drawn.

Methods Used: We performed a retrospective chart review of 42 pregnancies in women with SLE who received obstetrics care at University of Mississippi Medical Center between 2004 and 2006. Data was collected including prior pregnancies and complications, anticoagulant levels,

complement levels during pregnancy, medications and dosages, complications and outcomes, and analyzed to see if any correlations were noted.

Summary of Results: Of the 42 pregnancies we evaluated, 20 (47%) were preterm, 14 (33%) full term and 8 (19%) ended in fetal demise. Complications included 15 cases of preeclampsia, 14 cases of hypertension, 6 cases of PPROM, 3 cases of IUGR, 3 cases of oligohydramnios and 2 cases of HELLP syndrome. In addition, we found that of the 14 full term deliveries, 10 of these patients were taking hydroxychloroquine. Patients taking hydroxychloroquine in combination with prednisone also required lower dosages of prednisone (14mg to 21mg respectively). We also found the average dosage of prednisone in patients with hypertension or preeclampsia to be 18mg.

Conclusions: The results of our review showed a higher rate of preterm labor as well as fetal demise than previously reported in lupus pregnancy. This data likely reflects that our center is a tertiary referral center and is routinely receiving transfer of the sickest lupus patients. We did find, even in our small sample size, a significant advantage to hydroxychloroquine usage in pregnancy. While debated in the past, hydroxychloroquine use is now considered to be safe and in fact should be used in lupus pregnancy. We found that hydroxychloroquine while decreasing the concomitant dosage of prednisone and thus decreasing the risk of pregnancy induced hypertension also was associated with more full term pregnancies. We intend to expand our current data to include more pregnancies and see if this correlation continues.

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DEVELOPMENT OF SEVERE ATOPIC DISEASE IN CHILDREN AFTER CARDIAC TRANSPLANT

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Purpose of Study: Recent literature indicates increased incidence of atopic disease among children following solid organ transplantation. We have identified a case series of post-cardiac transplant pediatric patients with severe atopic disease.

Methods Used: Case review of 6 cardiac transplant patients followed for severe atopic disease in the Allergy/Immunology Clinic at Arkansas Children's Hospital.

Summary of Results: Six post cardiac transplant patients (50% male) with mean age of 5.5 years (range 3.6–12.3 years) were identified. Mean age at transplant was 5.1 months (range 1.2–15.2 months). All patients received initial immunosuppression with prednisolone for 6–8 months and at least two other immunosuppressive agents including: tacrolimus (2/6), azathioprine (2/6), mycophenolate (4/6), and cyclosporine (3/6). Five of six patients had ≥ 2 atopic disorders with atopic dermatitis being the most prevalent (5/6 with 2 refractory cases). Other disorders included multiple food allergies (4/6), moderate-severe persistent asthma (3/6), allergic rhinitis (2/6), and drug allergy (1/6). Median peak IgE was 258 kU/L (range 4.7–2296 kU/L) and median absolute eosinophil count one year after transplant was 745 kU/L (range 162–1400). Family history was positive for atopic disease in 5/6 patients. Four of six patients have recurrent infections, three requiring immunoglobulin replacement.

Conclusions: Further work is needed to define factors that influence development of post-transplant atopic disease in pediatric patients, including duration and type of immunosuppressive therapy, environmental exposures, dietary exposures, and recipient/donor atopic history.

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COMPLICATIONS OF ALLERGIC FUNGAL SINUSITIS

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Purpose of Study: Allergic fungal sinusitis (AFS) is a syndrome of chronic noninvasive fungal sinusitis resulting from a chronic hypersensitivity reaction to fungi in the paranasal sinuses. We followed a cohort of 21 patients with AFS and have observed four unusual complications.

Methods Used: With IRB approval, we reviewed medical records of 21 patients meeting published diagnostic criteria for AFS. Individuals who experienced complications of AFS, beyond the usual chronic rhinosinusitis with polyps, were identified and contrasted to those patients without such complications.

Summary of Results: Four patients had serious complications associated with expansion of allergic mucin out of the paranasal sinuses. These included:

1)AFS with concomitant ABPA 2)AFS with expansion into the orbital fissure requiring orbital exenteration 3)AFS with expansion into brain stem requiring craniotomy 4)AFS with otitis media and tympanic membrane perforation. The mean IgE level for the 4 patients with complications was 1590 IU (range 8,100) versus 597 IU (50-2323) for the remaining 17 patients without severe complications. The mean number of sinus surgeries performed in the patients with complications was 3.5 versus 2.3. All 4 patients responded well to surgery, corticosteroids, and fungal allergen immunotherapy.

Conclusions: AFS is a chronic disease resulting in the accumulation of large quantities of allergic mucin with the potential to expand outside the sinuses. To prevent complications, patients with this condition require long-term follow-up, longitudinal IgE determinations, surveillance rhinoscopy, and sinus imaging. Our results show that some individuals with AFS may present with major complications at the time of diagnosis.

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DO ADIPOCYTOKINES PLAY A ROLE IN BONE TURNOVER IN SPONDYLOARTHROPATHIES?

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Purpose of Study: To assess the role of adipocytokines in bone turnover in SpA patients; and to study the effects of treatment on inflammation and bone metabolism.

Methods Used: 30 adults SpA patients were studied; 18 /30 (60 %) Psoriatic Arthritis (PsA), 12/30 (40 %) Ankylosing Spondylitis (AS). Naïve to treatment 26.7%, DMARDs 20%, TNF Blockers 53.3% Mean age PsA 49.6 (11.0) , AS 51.6 (13.24) years; mean disease and treatment duration were PsA 172.75 (171.9),AS 151.16 (110) months and DMARDs 94.6 (103.8), TNF Blockers 63 (40.69), Naïve 0 month (PsA 22% DMARDs, 16.7% Naïve, 61.1% TNF Blockers; AS DMARDs 16.7%, Naïve 41.7%, TNF Blockers 41.7%). Clinical data, DEXA (lumbar spine and femur), X-R- Lumbar and Cervical Spine/Pelvis/SI joints, mSASSS, BASRI were assessed at the same time. A quantitative ELISA assay for IFN α / β / γ , sTNFRI /II, IL-1, s IL-1 R II,IL-12, IL-17,IL-23, IL-6, IL-15, EGF,s IL-6 R, Dkk-1,WIF,OPG, RANK was performed in duplicate. ANOVA with Tukey post-hoc analysis was used to compare biomarker levels between disease and treatment groups.

Summary of Results: The SpA naïve group had significantly higher mean levels of mSASSS (p= 0.025), IL-6 (p= 0.011), adiponectin (p=0.038), leptin (p=0.034), VEGF (p=0.027) and sTNFRI (p=0.028) compared to the other two groups. Differences in the pattern of associations emerged when the PsA were analyzed separately; the DMARDs group had significantly higher Z score hip (p=0.041), IFN β (p=0.031), and significantly lower sTNFRI (p=0.023). CRP was significantly higher in the AS (p=0.05). AS DMARDs, leptin (p=0.033) and IL-17 (0.012) were significantly higher.

Conclusions: This study shows the interplay of some of the mediators that participate in bone turnover for bone degradation- IL-6, sTNFRI; and adipocytokines leptin and adiponectin for formation/degradation. Long term use of DMARDs and TNF blockade appears to regulate mediators of bone turnover (adiponectin, IFN β), but larger number of patients are needed to fully assess this association.

**Cardiovascular I
Concurrent Session
2:00 PM**

Friday, February 26, 2010

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DUAL OXIDASE INVOLVEMENT IN ANGIOTENSIN II-INDUCED OXIDATIVE STRESS IN WASTED SKELETAL MUSCLE

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Purpose of Study: Congestive heart failure is a leading cause of cardiovascular mortality and morbidity and is associated with elevated circulating levels of angiotensin II (ANG) and muscle wasting, which is an important predictor of poor outcome. We have shown that ANG infusion in FVB mice increases oxidative stress and induces skeletal muscle wasting, however the oxidases mediating ANG-induced oxidative stress in mouse skeletal muscle were not identified yet.

Methods Used: Gastrocnemius muscle frozen sections were stained with superoxide-sensitive dye DHE with/without co-incubation with superoxide scavenger PEG-SOD to quantify total superoxide levels in FVB mice infused with 1 ug/kg ANG or vehicle (SHM) for 7 days. To distinguish NADPH oxidase- and mitochondria-dependent superoxides, part of muscle tissue was pre-incubated with 0.5 mM NADPH oxidase inhibitor apocynin and another part with 50 uM rotenone, mitochondria-derived superoxide blocker. "Pure" mitochondria-specific superoxides were quantified by sections staining with 5 uM MitoSox Red and mitochondrial content in skeletal muscle was evaluated by staining with 100 nM MitoTracker Green.

Summary of Results: ANG II increased total superoxide levels by 67 $\pm$ 7% compared to SHM (P<0.005) and pre-treatment with apocynin only partially blocked this effect (62% reduction compared to no inhibitor control, P<0.05). Since rotenone also partially reduced of ANG-induced superoxides (35% decrease vs. no inhibitor control), these data suggest that both NADPH oxidase and mitochondria mediate ANG-induced oxidative stress. ANG also increased "pure" mitochondrial superoxides as measured by staining with MitoSOX (35 $\pm$ 7% increase compared to SHM after normalization to PEG-SOD control or 55 $\pm$ 7% increase compared to SHM after normalization to rotenone-pre-treated section), however ANG did not change mitochondrial content in skeletal muscle. ANG II increased relative gene expression of two NADPH oxidase subunits: p22phox and p47phox (by 55% and 88%, respectively, real-time PCR) suggesting potential mechanism of ANG-induced NADPH oxidase activation.

Conclusions: Thus, we demonstrate that ANG increases superoxide formation in skeletal muscle through dual oxidase (NADPH oxidase and mitochondria) activation and this effect correlates with muscle wasting.

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HYPOKALEMIA AND HYPOMAGNESEMIA IN PATIENTS WITH ACUTE ONSET ATRIAL FIBRILLATION FOLLOWING SEVERE BURN INJURY

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Purpose of Study: A simultaneous dyshomeostasis of multiple macro- and micronutrients is found at the time of or within days of admission in patients with acute burn injury. This thermal trauma-induced dysequilibrium to their extracellular cationic composition includes hypocalcemia, together with severe hypozincemia and hyposelenemia. A subset of these patients are known to develop atrial fibrillation (AF) during their hospitalization, although its etiologic origin(s) are not clear. We examined serum K⁺ and Mg²⁺ obtained in patients with acute burn injury and who developed AF to explore the potential missing link between AF and the presence or absence of hypokalemia and/or hypomagnesemia.

Methods Used: From a cohort of 187 patients (117M; 45 $\pm$ 2yrs), consecutively admitted to the Burn Unit of an urban medical center over the course of 3 yrs, 33 patients (20M; 61 $\pm$ 3 yrs) developed electrocardiographic evidence of sustained AF. In this retrospective study, we examined the medical records of these patients for serum K⁺ and Mg²⁺.

Summary of Results: Using stringent criteria for serum K⁺ $\leq$ 3.6 mEq/L and Mg²⁺ $\leq$ 1.8 mg/dL in this cohort with acute AF and severe burn injury, we found hypokalemia (3.4 $\pm$ 0.1 mEq/L) and hypomagnesemia (1.6 $\pm$ 0.1 mg/dL) in 30 (90%) of the 33 patients with AF.

Conclusions: In patients hospitalized with severe burn injury and in whom acute AF develops, hypokalemia and hypomagnesemia are common. Serum electrolytes must be carefully monitored and, when appropriate, abnormal electrolytes promptly corrected with the view toward the prevention or correction of acute onset AF. Thus, in addition to monitoring for the derangements in macro- and micronutrients that accompany acute burn injury, abnormal serum electrolytes and their impact on cardiac rhythm also need to be considered and, when necessary, therapeutically addressed.

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DISRUPTION OF TRANSFORMING GROWTH FACTOR β (TGF β) SIGNALING BLOCKS PRESSURE OVERLOAD-INDUCED DOWNREGULATION OF ENDOGENOUS PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR γ (PPAR γ) EXPRESSION IN HEART

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Purpose of Study: PPAR γ activators modulate extracellular matrix (ECM) molecules expression in cardiac fibroblasts (CFs), which could attenuate myocardial fibrosis in the pressure overloaded heart. This study utilized a transgenic mouse model that expresses an inducible dominant negative mutation of the TGF β type II receptor (DnTGF β RII) to test the hypothesis that PPAR γ expression is reduced in the pressure overload heart and that TGF β signaling is required for the pressure overload-induced down-regulation of PPAR γ expression.

Methods Used: 1) In vivo: 10 wk old male DnTGF β RII and nontransgenic (NTG) mice were given 25 mM Zn⁺⁺ in drinking water 1 wk prior to transverse aortic constriction (TAC) to induce expression of the DnTGF β RII gene. PPAR γ protein levels in left ventricles (LV) were assessed 1 wk after TAC. 2) In vitro: Mouse CFs were transfected with a PPAR γ promoter+ luciferase reporter plasmid and exposed to TGF β 1 (1 ng/ml) for 24 hrs. PPAR γ promoter activity, mRNA and protein levels were assessed. Chromatin immunoprecipitation (ChIP) assay was used for detection of binding of Smad proteins and a transcriptional co-repressor and co-activator on the PPAR γ promoter.

Summary of Results: TAC decreased LV PPAR γ protein levels in TAC-NTG mice. In contrast, PPAR γ protein levels were increased in LV of DnTGF β RII mice when TGF β signaling was disrupted. TGF β 1 treatment decreased PPAR γ promoter activity ($\downarrow$ 53%), mRNA ($\downarrow$ 34%) and protein ($\downarrow$ 52%) levels in CFs. Activation of TGF- β signaling significantly increased binding of Smad2/3, Smad4 and histone deacetylase-1 (HDAC1, a transcriptional co-repressor), and decreased binding of acetylated histone 3 (AcH3, a transcriptional co-activator) to the promoter region of the PPAR γ gene.

Conclusions: These data indicate that TGF β 1 enhances Smad2/3/4 binding to the PPAR γ promoter and that this coincides with increased HDAC-1 and decreased AcH3 binding, as well as decreased expression of the PPAR γ gene in CFs. The finding that TGF β 1 can directly suppress PPAR γ expression in CFs via a transcriptional mechanism suggests that inhibition of PPAR γ expression may be a novel mechanism of TGF β -mediated cardiac fibrosis.

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DOWNREGULATION OF PRO-ATHEROGENIC 12/15-LIPOXYGENASE GIVES INSIGHT TO MECHANISM OF IGF-1 INDUCED ATHEROPROTECTION

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Purpose of Study: We have shown that Insulin-like Growth Factor I (IGF-1) infusion into ApoE^{-/-} mice suppresses atherosclerosis. 12/15-lipoxygenase (LOX) plays a major role in oxidation of native LDL to its proatherogenic form oxidized low density lipoprotein (OxLDL) and is expressed in vascular smooth muscle cells (SMC) and macrophages (M Φ). The purpose of this study was to obtain insight in the potential role of SMC vs. M Φ LOX in IGF-1-induced atheroprotection.

Methods Used: ApoE^{-/-} mice were injected with IGF-1 (1.8 mg/kg/d, 1 wk) or chronically infused (1.5 mg/kg/day, 12 wk). Aortic LOX expression was measured by RT-PCR, immunostaining, plaque superoxides by DHE, and M Φ infiltration by Mac3 staining. To obtain insight into the relative role of SMC vs. M Φ LOX in IGF-1-induced atheroprotection we generated SMP8/ApoE^{-/-} mice in which IGF-1 is overexpressed in SMC. SMC or M Φ were exposed to IGF-1 (10 ng/ml, 50 ng/ml, 24h) and LOX gene expression was analyzed. SMC or M Φ were exposed to OxLDL or native LDL (control, 80 μ g/ml, 16 h) and 14,15-leukotriene (a product of LOX-specific enzymatic reaction) levels were measured in conditioned media by ELISA.

Summary of Results: Acute IGF-1 decreased LOX aortic gene expression by 64 $\pm$ 6%. ApoE^{-/-} mice had a 77 $\pm$ 6% increase in plaque superoxides vs. adjacent media, $P < 0.05$, correlating with increased M Φ infiltration and LOX expression. Chronic IGF-1 infusion markedly reduced atherosclerotic lesion size (28% decrease, $P < 0.05$), aortic plaque LOX immunopositivity (74 $\pm$ 9% decrease, $P < 0.05$), and superoxide levels (84 $\pm$ 7%, $P < 0.05$). SMP8 mice had decreased aortic LOX expression (71% decrease vs. ApoE^{-/-} mice, $P < 0.05$). Similarly, IGF-1 dose-dependently decreased LOX gene expression in M Φ . OxLDL induced a dramatic increase in LOX activity levels in M Φ and SMC, but IGF-1 completely abolished OxLDL-induced LOX activation only in M Φ .

Conclusions: In summary, IGF-1 infusion markedly reduces atherosclerotic plaque burden and LOX levels, but SMC-specific IGF-1 over expression reduces LOX but does not alter atherosclerosis. Considering that IGF-1 markedly inhibits OxLDL-induced LOX activation in M Φ in vitro, our data

suggest that IGF-1 down regulation of M Φ LOX activity plays an important role in atheroprotection.

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HYPOKALEMIA AND HYPOMAGNESEMIA WITH PROLONGED QT_c OR ATRIAL FIBRILLATION IN HOSPITALIZED PATIENTS

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Purpose of Study: Atrial fibrillation (AF) is a major health problem. The identification of factors predisposing to AF that are reversible, such as hypokalemia and hypomagnesemia with prolonged QT_c, are therefore of considerable importance in the prevention and/or correction of AF.

Methods Used: Interrogation of routine ECGs during May-June, 2009, revealed 40 patients (25M; 54 $\pm$ 2 yrs), hospitalized at an urban medical center with or without cardiovascular disease, to have prolonged QT_c ($\geq$ 460 ms) or AF/flutter. We retrospectively examined for serum electrolytes, including Mg²⁺, that had been obtained in these patients. We also addressed whether these patients were reported to have emesis/diarrhea, alcohol abuse, or if receiving diuretics or medications known to prolong QT_c. Patients were not known to have: cirrhosis; diabetic ketoacidosis; metabolic disorders associated with electrolyte disturbances, including the syndromes of Cushing, Conn, Gitelman or Bartter; renal tubular acidosis; an intestinal or biliary fistula; nasogastric suction; or thyroid disease.

Summary of Results: Based on evaluation of routine ECG, 26 patients (14M; 51 $\pm$ 2 yrs) had prolonged QT_c (501 $\pm$ 7 ms) alone and 14 (11M; 60 $\pm$ 5 yrs) AF/flutter. Mean $\pm$ SEM values are shown below. Using stringent criteria, hypokalemia ($<$ 4.0 mEq/L) was present in 75% of these 40 patients, 58% had hypomagnesemia ($<$ 2.0 mg/dL), and 50% had both hypokalemia and hypomagnesemia, without hyponatremia, hypochloremia or a metabolic alkalosis. Mild to moderate hypokalemia ($\leq$ 3.6) and hypomagnesemia ($\leq$ 1.8) were found in 58% and 40%, respectively; 53% were receiving a thiazide or loop diuretic. Emesis/diarrhea was present in 7%, alcohol abuse in 18%, and 35% were receiving a drug that could prolong QT_c.

Conclusions: In hospitalized patients who on routine ECG are found to have prolonged QT_c or AF/flutter, it is clinically prudent to carefully evaluate for hypokalemia and hypomagnesemia, often related to adjuvant diuretic treatment, and whose reversal could favorably contribute to the prevention or correction of AF.

	Na ⁺	K ⁺	Cl ⁻	HCO ₃	Mg ²⁺
Prolonged QT _c	137 $\pm$ 1	3.6 $\pm$ 0.1	99 $\pm$ 4	25 $\pm$ 1	1.9 $\pm$ 0.1
AF/flutter	136 $\pm$ 1	3.6 $\pm$ 0.1	101 $\pm$ 1	26 $\pm$ 1	1.9 $\pm$ 0.1

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FOXO TRANSCRIPTION FACTOR ACTIVATION IN DIABETIC CARDIOMYOPATHY

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Purpose of Study: FoxO transcription factors govern numerous events involved in cell growth, survival, and metabolism. We have shown previously that FoxO, which is regulated by the insulin-Akt pathway, remains persistently active in load-stressed myocardium, contributing to the insulin resistance of hypertrophied myocytes. Also, we have found that FoxO activation in heart is elevated in a model of diabetes (db/db) but decreased in animals exposed to a high-fat diet (HFD). These findings led us to hypothesize that abnormal activation of FoxO transcription factors contributes to insulin resistance in the myocardium and participates in the pathogenesis of diabetic cardiomyopathy.

Methods Used: To test this, we evaluated cardiac FoxO activity in response to insulin stimulation in 10-12 week old, obese (ob/ob) and diabetic mice (db/db), and in mice fed a 60% fat diet (HFD). Insulin was administered, and hearts and livers were harvested at 5 minutes post-injection (a time selected based on time course analyses). Finally, we ran western blots using heart and liver samples, and densitometry to quantify our results.

Summary of Results: Inactive, phosphorylated FoxO levels were significantly lower in diabetic (db/db) and obese (ob/ob) mice, pointing to the presence of relatively higher levels of active (non-phosphorylated) FoxO. Akt in its activated form (P-Akt) inactivates FoxO; we found that P-Akt levels were consistently lower in db/db and ob/ob hearts. Consistent with over-activation of FoxO, we detected significantly increased amounts of multiple

FoxO downstream targets (Atrogin-1, p21, MURF) in hearts from db/db and ob/ob mice. Qualitatively similar findings were observed in hearts harvested from HFD mice, although the relative magnitude of activation were lower.

Conclusions: These findings lend additional support to a model where FoxO activation is elevated in diabetic cardiomyopathy, contributing to myocyte insulin resistance and long-term pathological remodeling.

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REGIONAL HETEROGENEITY IN MYOCARDIAL CALCIUM AND ZINC CONTENT FOLLOWING ISOPROTERENOL-INDUCED INJURY IN RATS

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Purpose of Study: Cardiomyocyte intracellular Ca^{2+} overloading leads to an induction of oxidative stress, together with an opening of the mitochondrial permeability transition pore. The ensuing necrosis is followed by a replacement fibrosis, or myocardial scarring. Chronic excessive intracellular Ca^{2+} accumulation (EICA) is intrinsically coupled to intracellular Zn^{2+} entry, where Zn^{2+} acts as antioxidant facilitated by the upregulated expression of Zn^{2+} transporters and metallothionein, a Zn^{2+} -binding protein (Kamalov G, et al. *J Cardiovasc Pharmacol* 2009;53:414–423). In acute catecholamine excess, myocyte necrosis occurs within hours, not allowing for counterregulatory Zn^{2+} responses. Moreover, subsequent microscopic scarring is distributed in a heterogenous pattern favoring the left ventricular (LV) apex and right ventricle (RV) to suggest a differential spatial susceptibility to necrosis.

Methods Used: Using atomic absorption spectroscopy we examined myocardial Ca^{2+} and Zn^{2+} concentrations in different regions of the rat heart appearing at 8h following subcutaneous isoproterenol administration (Isop, 1 mg/kg): epi- and endocardium of the LV base, equator and apex; together with full thickness RV.

Summary of Results: As noted below and compared to controls, a marked ($*p<0.01$) Ca^{2+} overloading, coupled to Zn^{2+} depletion, was seen in the RV and the LV apex (endocardium>epicardium); no significant EICA was found at the LV equator or base and there was no Zn loss at these sites (data not shown).

Conclusions: A heterogeneity in myocardial Ca^{2+} overloading and Zn^{2+} depletion was found at 8h following Isop treatment and which favored the RV and LV apex, particularly its endocardium. This may explain the known predilection for myocardial scarring at these sites. Mechanisms accounting for this differential EICA and susceptibility to necrosis remain to be elucidated.

Myocardial Sites	Control	Isoproterenol (8 hr)
RV Ca^{2+} (nEq/mg)	8.18±0.58	17.18±3.70*
RV Zn^{2+} (ng/mg)	83.54±1.39	78.92±0.42*
LV apex endocardium Ca^{2+}	10.05±0.46	18.09±2.66*
LV apex epicardium Ca^{2+}	8.67±0.83	16.41±1.71*
LV apex endocardium Zn^{2+}	83.47±0.87	77.35±1.27*
LV apex epicardium Zn^{2+}	84.04±1.3616	76.80±1.92*

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LOW SERUM INSULIN-LIKE GROWTH FACTOR 1 POTENTIATES ATHEROCLEROTIC PLAQUE DEVELOPMENT IN APOE KNOCKOUT MICE: POTENTIAL MECHANISM OF ACCELERATED ATHEROSCLEROSIS IN AGING

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Purpose of Study: Aging is associated with a reduction in serum insulin-like growth factor-1 (IGF-1) levels and an increased risk of atherosclerosis, but whether lower IGF-1 plays a causative role is unknown. This study is aimed to obtain insights into the relation between circulating IGF-1 levels and atherosclerotic burden independent of age.

Methods Used: A congenic mouse strain with a 20% reduction in circulating IGF-1 (C3H.B6-6T [6T]) was bred into the ApoE knockout (ApoE KO) background to obtain the C3H.6T^{+/+}/ApoE KO (6T/E) mouse to mimic the clinical state of low circulating IGF-1 and to study its effect on atherosclerosis development.

Summary of Results: Serum IGF-1 levels in 6T/E mice were similar to those of 6T (6T/E: 208.81 ± 58.33 ng/ml vs 6T: 221.41 ± 58.33 ng/ml, $p=0.6$); but lower than those of ApoE KO (354.49 ± 76.33 ng/ml, $p<0.01$). Mice of all 3 groups (6T/E, 6T and ApoE KO) at 8 weeks old were fed with normal chow (NC) or western diet (WD) for 12 weeks and en face whole aortas were stained with Oil Red O. Results showed that (1) the NC-fed 6T/E mice developed more plaques than ApoE KO mice (% total plaque/aorta, 6T/E: 7.54 ± 2.21, ApoE KO : 4.91 ± 3.18, $p<0.018$); (2) when fed with the WD, the 6T/E also developed more plaques than the ApoE KO (6T/E: 14.87 ± 8.81, ApoE KO : 8.71 ± 3.13, $p=0.0005$). (3) There was no difference in body weight gain or blood pressure between the 6T/E or ApoE KO mice.

Conclusions: A novel atherosclerosis-prone mouse model that mimics age-related low circulating IGF-1 levels has been created. In these mice, a decrease in serum IGF-1 is accompanied by a diet-independent increase in aortic atherosclerosis. These results are consistent with epidemiological data indicating that lower IGF-1 levels are associated with an increased risk for ischemic heart disease and strongly support the rationale for development of new IGF-1-based therapies against atherosclerosis.

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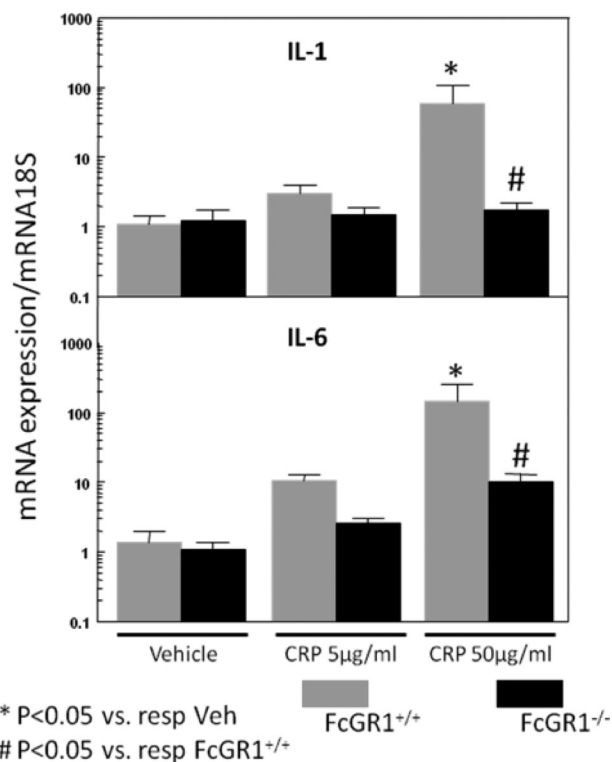
C-REACTIVE PROTEIN DRIVES INFLAMMATORY MEDIATOR EXPRESSION IN MOUSE MACROPHAGES VIA AN FCγRI RECEPTOR DEPENDENT PATHWAY

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Purpose of Study: In human C-reactive protein transgenic mice (CRPtg), the exaggerated response to vascular injury provoked by CRP is dependent on FcγRI. Since CRP co-localizes with F4/80 on the surface of macrophages in the lesion, we hypothesized that CRP stimulates inflammatory mediator expression by macrophages in vitro via the FcγRI receptor.

Methods Used: To test this hypothesis, bone marrow was harvested from wildtype and FcγRI^{-/-} mice and the cells were grown in culture with M-CSF. After 7 days, the cells were >90% positive for F4/80 and were treated with vehicle or CRP (5 or 50 μg/ml). RT-PCR was used to measure inflammatory mediator expression.

Summary of Results: In macrophages that expressed FcγRI, there was a dose-dependent increase in the expression of TNF-α, IL-1, IL-6, and IL-8 with CRP; the high dose (50 μg/ml) induced an 8, 53, 107, and 46-fold



increase in the expression of these cytokines, respectively (Fig; note log scale). In macrophages derived from FcγRI^{-/-} mice there was a diminished response to CRP treatment with the expression of these cytokines increasing by 6, 1.4, 9, and 18-fold, respectively.

Conclusions: CRP enhances the expression of inflammatory mediators by mouse macrophages in vitro. This effect is greatly diminished in cells that do not express the FcγRI receptor, suggesting that CRP drives inflammation via a cell signaling pathway that is dependent on the FcγRI receptor.

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INJECTED STIMULATED MULTIPOTENT STROMAL CELL WITH EGF ENHANCES ISCHEMIA-INDUCED VASCULOGENESIS IN TYPE 2 DIABETES

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Purpose of Study: Chronic tissue ischemia due to defective vascular perfusion is a marker of peripheral artery disease for which minimal therapeutic options exist. Thus, type 2 diabetes is characterized with altered stem cells and vasculogenesis. Because of the capability of stem cells to differentiate into vascular cells and the importance of epidermal growth factor (EGF) in angiogenesis, their critical role in the treatment of type 2 diabetic patients with ischemia peripheral artery disease may be as prophylactic agents preventing tissue damage by stimulating vasculogenesis. Therefore we determined if multipotent stromal cells (MSC) tagged with enhanced green fluorescent protein (EGFP) stimulated with or without exogenous EGF would improve vasculogenesis in ischemia hind limb of type 2 diabetic (db/db-) mice.

Methods Used: Ischemia was induced in the hind limb of db/db- mice and control for 28 days. EGFP-MSC stimulated with or without exogenous EGF (10 ng/ml) for 24 hr were locally injected in the mice hind limb once a week for 4 weeks. After 4 weeks, blood flow measured with MoorLDI-Laser and angiogenesis assessed with X-ray were completely recovered in control mice compared to db/db- mice.

Summary of Results: Isolated bone marrow from db/db- mice showed an increase in oxidative stress and reduction in Akt compared to control. Interestingly db/db- mice display a significant improvement of blood flow (60% and 96%) and vasculogenesis (61% and 98%) when treated with MSC or MSC pre-stimulated with exogenous EGF, respectively. Western blot analysis on hind limb muscles revealed an increase in phosphorylated Akt and VEGF receptor in db/db- mice injected with MSC or MSC+EGF compared to non-treated db/db- mice. Fluorescent microscopy images indicate that EGFP-MSCs differentiate into new microvessels. In vitro studies showed that adhesion and migration of MSC on cultured microvascular endothelial cells were elevated when MSC were pre-stimulated with EGF compared to non-stimulated MSC.

Conclusions: Our novel data provide evidence that in type 2 diabetes, MSC stimulated with EGF are able to significantly improve, better than MSC alone, the formation of microvessels in response to ischemia.

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HIGH FRUCTOSE FEEDING CAUSES STIFFER ARTERIES IN SPRAGUE-DAWLEY RATS

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Purpose of Study: It is not yet known if high fructose feeding has the potential to worsen the pulsatile nature of blood flows in arteries. Hence, the aim of the present study was to determine the effect of fructose on the mechanical properties of the rat arterial system.

Methods Used: Sprague-Dawley rats (n=16) were randomized into two groups viz. control and fructose fed (FF). FF rats were given 20% fructose solution while controls received tap water ad libitum for 8 weeks. Fasting (FG) and non-fasting (NFG) blood glucose, body weight (BW), systolic blood pressure (SBP) and heart rate (HR) were followed weekly throughout the feeding period. Oral glucose tolerance test was used to assess insulin resistance in these rats. Pulse wave velocity (PWV) and augmentation index (AI) was used as the markers of vascular stiffness. At the end of 8 weeks, animals were anesthetized (pentobarbitone, 60 mg/kg i.p.). Right carotid artery was catheterized and the catheter was advanced up to aortic arch and

another catheter was introduced through the left iliac artery and advanced up to abdominal aorta. The animal was allowed to stabilize and blood pressure was recorded simultaneously from carotid and iliac arteries.

Summary of Results: At the end of 8-week period, the fasting plasma glucose as well as plasma glucose after an oral glucose load were markedly higher in FF rats (FG, 5.2±0.3 mmol/l; NFG, 8.7±0.5 mmol/l) compared to control (FG, 4±0.2 mmol/l; NFG, 7.3±0.4 mmol/l). It is observed that in FF rats there was marked increase in BW (322±6g) and SBP (143±6 mmHg) compared to control (BW, 281±7 g; SBP, 105±4 mmHg) (all P<0.05). Moreover, PWV and AI in FF rats were markedly higher (PWV, 6.01±0.15 m/s and AI, 0.113±0.02) than control (PWV, 5.46±0.13 m/s and AI, 0.052±0.008).

Conclusions: These data suggested that 8 weeks feeding of high fructose not only resulted in hyperglycemia and mild elevation in blood pressure but also caused stiffening of arteries in rat.

Endocrinology and Metabolism

Concurrent Session

2:00 PM

Friday, February 26, 2010

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DOES ANTI-TNF-α THERAPY FOR AUTOIMMUNE DISORDERS IMPROVE GLUCOSE CONTROL IN DM 2 PATIENTS?

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Purpose of Study: Purpose of Study: DM 2 is associated with insulin resistance (IR), which is caused in part by the cytokine Tumor Necrosis Factor-α (TNF-α), produced in inflammatory fat tissue in muscle, liver, and adipose tissue itself. We assessed the effects of anti-TNF-α treatment on control of DM 2 in patients receiving this treatment.

Methods Used: Eight patients with Rheumatoid Arthritis (RA) or Crohn's Disease (CR) and DM 2 were studied by retrospective chart review in VA using CPRS, before and after anti-TNF-α therapy. A matched group of patients with both diagnoses, but not on anti-TNF-α therapy, was also studied and used as an external control. We assessed control of DM by FBS, HgA1c and fasting plasma triglyceride (TG) values. Student's "t" test, paired and unpaired, and linear regression analysis were utilized.

Summary of Results: Eight patients had an average FBS of 142 mg% before treatment; after initiation of treatment, the average FBS was 126 mg%, p < 0.01; and in the last full year of treatment, FBS was 121 mg%, p<0.01. Similarly, when FBS was plotted after 8–10 years on anti-TNF-α therapy, and the line plot compared to a matched control population, the statistical difference, using General Linear Model Analysis was p < 0.01. In select cases, average HgA1c was 6.5 % before, and 5.5 % after treatment, and TGs were 350 mg / dl before, versus 200 mg/dl, after therapy. In the matched control patient population, these parameters were either increased or maintained, but not decreased as was seen in treated patients.

Conclusions: In a retrospective study, patients with RA or CR and DM 2, who also were receiving anti-TNF-α treatment for their auto-immune disease, had significant improvement in their FBS, HgA1c, and TG values when compared to themselves (before treatment) and to matched untreated controls. Knowing that TNF-α is produced by oxidative stress in fat imbedded in skeletal muscle and liver, these results make a powerful case for endogenous TNF-α being a causative factor in IR of DM 2.

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EFFECTS OF A HIGH PROTEIN COMPARED TO A HIGH CARBOHYDRATE DIET ON VARIOUS MARKERS OF OXIDATIVE STRESS AND LIPID METABOLISM

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Purpose of Study: It has been well established that weight reduction improves disease outcomes, but the optimal diet to achieve weight loss and positively influence metabolic markers need further investigation. The purpose of our study was to observe the effects of a moderately high protein (HP) diet composed of 30% protein, 40% carbohydrates, and 30% fat

compared to a high carbohydrate (American Diabetes Association) (HC) diet composed of 15% protein, 55 % carbohydrates and 30% fat on women with regard to weight loss and other metabolic parameters.

Methods Used: Women between the age of 20 and 45 years with a BMI > 30 and normal oral glucose tolerance tests (OGTT) were placed on either a HP or a HC for a six-month period. Various measurements were taken to evaluate the effects of the diet: weight, waist circumference (WC), body mass index (BMI), blood pressure, fasting blood glucose, 2 hour blood glucose following an OGTT and mixed meal tolerance test (MMT), lipids and oxidative stress markers (i.e. dichlorofluorescein (DCF) and lipid peroxidation (MDA)).

Summary of Results: In this study we report results of 8 subjects (4 HP and 4 HC) after one month of being on the diets. Subjects on both the HP and HC diets demonstrated decreased weight, WC, blood pressure and fasting glucose and lipid levels with a greater decrease in the HP diet group. No significant difference was observed in the 2-hour post-prandial glucose response to either HP or HC MMT after one month on the diets. Markers of oxidative stress and lipid peroxidation at 2 hour MMT was less in the HP than the HC diet.

Conclusions: In conclusion, both HP and HC diet subjects lost weight over the first 4 weeks of the study since both were caloric restriction. These initial results of the study indicate that the HP diet may be a more beneficial diet for weight loss and reducing oxidative stress and lipid peroxidation as well as being a nutritious and palatable diet for possible long term use.

Diet	Δ Weight lbs	Δ WC	Δ ASP	Δ Glucose mg/dl Fasting	Δ Glucose mg/dl 2 hr PP	Δ TG mg/dl Fasting	Δ TG mg/dl 2 hr PP	Δ DCF uM	Δ MDA uM
HP	-8.1	-2.9	-8	-5.2	-1.3	-10	-2	-0.8	-0.4
HC	-5.1	-2.4	-6	-2.1	-0.9	-8	-2	-0.2	-0.1

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PRO-INFLAMMATORY CYTOKINES IN GLYCEMIC EXCURSIONS:

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Purpose of Study: We have documented that hyperglycemic crises of diabetic ketoacidosis and non-ketotic hyperglycemia are associated with production of counter-regulatory hormones and pro-inflammatory cytokines. In our recent study, we also documented that hypoglycemia is associated with elevation of pro-inflammatory cytokines. In this review, we attempted to compare the pro-inflammatory cytokines and counter-regulatory hormones in the hypo and hyperglycemic crisis.

Methods Used: In our initial study, in order to investigate if hyperglycemia could evoke pro-inflammatory responses, we measured glucose, cortisol, epinephrine, norepinephrine (NEP), growth hormone (GH), pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, IL-8), CRP, Free Fatty Acids (FFA) and leukocytosis at baseline and after resolution of hyperglycemic crises in 58 patients with diabetic ketoacidosis or non-ketotic hyperglycemia. To evaluate the effect of hypoglycemia on pro-inflammatory cytokines, we induced hypoglycemic stress in thirteen healthy male subjects and measured above mentioned parameters.

TABLE 1. Measured pro-inflammatory cytokines and counter-regulatory hormones in hypo and hyperglycemia. (mean±SD)

Parameters	Hypoglycemia	hyperglycemia
CRP (mg/l)	7.0 ± 2.0	51 ± 3
TNFα (μg/ml)	11.1 ± 3.6	22.7 ± 3.6
IL6 (μg/ml)	4.1 ± 1.6	14.9 ± 2.6
IL8 (μg/ml)	18.8 ± 7.7	29.3 ± 3.5
IL1β (μg/ml)	2.4 ± 1.7	9.8 ± 2.3
FFA (mM)	0.5 → 1.1	1.6 ± 0.1
Glucose (mg/dl)	38 ± 20	453 ± 45
Cortisol (μg/dl)	15.23 ± 5.8	46.2 ± 2.3
GH (ng/ml)	27.3 ± 17.6	12.2 ± 2.2
NEP (pg/ml)	686 ± 172	1095 ± 20
Epinephrine (pg/ml)	1116 ± 102	120 ± 5
Leukocytes (x103/μl)	12.9 ± 2	14.4 ± 0.7

Summary of Results: The comparisons of measured parameters are shown in table 1.

Conclusions: We have demonstrated that acute hypoglycemia and hyperglycemic crises could similarly provoke elevation of pro-inflammatory cytokines and counter-regulatory hormones. However, quantitatively, hyperglycemia produces greater level of these measured parameters. This could be possibly explained by the fact that duration of hyperglycemic crises was longer than hypoglycemia.

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EFFECTS OF INTRAVENOUS AND ORAL FAT LOAD ON BLOOD PRESSURE, ENDOTHELIAL FUNCTION, AND SYMPATHETIC ACTIVITY IN OBESE SUBJECTS

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Purpose of Study: We previously reported that increasing free fatty acids (FFA) via intravenous infusion of Intralipid for 48 hours results in elevated blood pressure (BP), endothelial dysfunction, and increased markers of inflammation in normotensive patients with diabetes mellitus. Presently, we compared the effects of intravenous (IV) and oral (PO) fat load on BP, endothelial function, and sympathetic activity in healthy, obese subjects.

Methods Used: 13 healthy subjects [mean age 32 yrs, BMI 37 kg/m², fasting blood glucose 91 mg/dl, BP 113/66 mm Hg] underwent, in random order, 5 admissions for 8-hour infusions of saline 40 ml/hr (control), IV Intralipid 20% at 20 mL/h (32 g) or 40 mL/h (64 g), and low (25 g) or high (60 g) oral fat load. During each fat load, BP and FFA were measured every 2 hours and heart rate variability (HRV), flow-mediated dilatation (FMD), and pulse-wave analysis (PWA) were performed every 4 hours.

Summary of Results: FFA and BP, HRV, FMD, and PWA did not change during the saline infusion. IV fat load increased FFA from 0.85 to 1.52 mmol/L (P<0.001) in 20 ml/hr group and from 1.0 to 2.0 mmol/L in 40 ml/hr (P<0.01); these changes were associated with marked time-dependent elevation of systolic BP up to 12-14 mm Hg (P<0.05) but no changes in HRV or PWA. Compared to baseline, FMD decreased by 25% (P<0.01) and 22% (P<0.01) at 4 and 8 hours, respectively, in the IV 20 ml/hr group and by 33% (P<0.05) only at 4 hours in the IV 40 ml/hr group. FFA did not change in the low PO fat group but increased from 0.97 to 1.43 mmol/L by 8 hours of the study after high PO fat (P<0.01). Both low and high oral fat load increased systolic BP by 6-13 mm Hg compared with baseline (P<0.05). Low PO fat but not high PO fat diminished FMD by 20% (P<0.05) compared to baseline. Changes in HRV and PWA were not statistically significant between low and high PO fat load groups.

Conclusions: Intravenous and oral fat load led to consistent increases in systolic BP and altered endothelial function, but not in markers of sympathetic activity. Further studies are needed to determine the underlying mechanisms of fat load-induced hypertension and endothelial dysfunction in obese subjects.

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ALTERED PLASMA CYTOKINE AND ADIPOKINE LEVELS IN DIABETES MELLITUS

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Purpose of Study: Plasma cytokines and adipokines are involved in inflammation, endothelial dysfunction, insulin resistance and atherogenesis and have been implicated in the progression of diabetes and its complications. The goal of current study was to assess levels of plasma cytokines and adipokines in Type 1 and Type 2 diabetic patients.

Methods Used: There were four groups of patients: Type 1 and Type 2 diabetic patients and corresponding age-matched controls (20 male patients per group). Age: Type 1: 48±14 (yr, mean ± SD), Controls: 48±14; Type 2: 51±9, Controls: 50±9. HbA1c: Type 1: 8.6±2.0%, Controls: 5.2±0.3%; Type 2: 7.4±1.5%, Controls: 5.2±0.3%. Cytokines and adipokines were measured by enzyme-linked immunosorbent assay (ELISA) and included a biomarker of inflammation (C-reactive protein: CRP), markers of endothelial cell activation (vascular cell adhesion molecule-1: VCAM-1; intercellular adhesion molecular-1: ICAM-1), and biomarkers of insulin resistance and atherogenesis including plasminogen activator inhibitor (PAI-1), adiponectin, leptin, and leptin:adiponectin (L/A) ratio.

Summary of Results: Type 1 diabetic patients showed higher levels of adiponectin ($p<0.001$), similar levels of PAI-1, leptin, VCAM-1, ICAM-1 and CRP vs. controls; their L/A ratio was lower than controls ($p<0.05$). In contrast, Type 2 diabetic patients showed similar levels of adiponectin, PAI-1 and VCAM-1, and higher levels of leptin ($p<0.05$), CRP ($p<0.05$), and ICAM-1 ($p=0.07$) than controls. Their L/A was higher than controls, although this did not reach significance ($p=0.1$).

Conclusions: Different patterns of L/A and cytokine and adipokine levels in Types 1 and 2 diabetes may be due to altered metabolic homeostasis including various degrees of inflammation, endothelial dysfunction, insulin resistance and atherosclerosis, but confirmatory studies are needed.

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VITAMIN D25(OH) IN AN OBESE PEDIATRIC POPULATION LIVING BELOW 35 DEGREE LATITUDE DURING THE SUMMER

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Purpose of Study: Hypovitaminose D25(OH) has been demonstrated in the pediatric and adult population. The most recent NHANES indicates that 9% of the pediatric population is deficient (Vitamin D25(OH) <15 ng/dl) and up to 60% are insufficient (>15 ng/dl but <30 ng/dl). Populations living in areas above 35 degrees latitude have decreased Vitamin D synthesis between November and March. Seasonal variation also impacts the Vitamin D status. African American patients are also more likely to be insufficient. Hypovitaminose D is positively correlated to T2DM and cardiovascular risk but no recommendations for screening or treatment have been formulated. Our hypothesis states that in a population of obese (>95 th %ile) children, Vitamin D25(OH) deficiency (<15 ng/dl) is more prevalent than in the general population even in optimal sunlight exposure (below a latitude of 35 degrees).

Methods Used: A retrospective analysis of the charts of patients seen in the PHLC from April 1, 2009 through September 30, 2009 was done. Vitamin D25(OH) data were extracted. Other data included anthropometrics and demographics.

Summary of Results: Out of 402 records, 172 patients had a Vitamin D25(OH) level. Hypovitaminose D was present in 83% (21% deficient, 62% were insufficient). Vitamin D deficiency and insufficiency were significantly different in females and African Americans. The BMI and ages were significantly different between the deficient group and the insufficient or normal group; however they were not significantly different between the insufficient and normal group.

Conclusions: In our obese pediatric population, the prevalence of abnormal Vitamin D25(OH) (insufficient and deficient) is greater than the expected percentages in the overall population. This prevalence is occurring even in the optimal situation of sunlight exposure. Moreover, Vitamin D25(OH) levels are significantly lower in higher BMI, females and African Americans. In view of the risks associated with hypovitaminose D, we propose that all children with obesity be screened for Vitamin D25(OH) level.

	N	Average Vitamin D 25(OH) ng/dl $\pm$ sd	% of Patients	Average Age (in years) $\pm$ sd	Female (N(%))	African American (N(%))	Average BMI (kg/m2) $\pm$ sd
Patients all	172	23.4 $\pm$ 10.7	----	13 $\pm$ 4	110(64%)	114(66%)	35.6 $\pm$ 10.0
Vit D25(OH) ≥ 30 ng/dl	36	39.3 $\pm$ 9.2	21%	12 $\pm$ 5	18(50%)	12(30%)	34.6 $\pm$ 9.1
Vit D25(OH) insufficient (<29 ng/dl, >15 ng/dl)	106	21.5 $\pm$ 4.3	62%	12 $\pm$ 4	69(65%)	75 (71%)	34.3 $\pm$ 8.6
Vit D25(OH) deficient (<15 ng/dl)	30	10.8 $\pm$ 2.8	17%	15 $\pm$ 3	23(78%)	27(90%)	41.4 $\pm$ 13.2

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VITAMIN D SUPPLEMENTATION IN THE BREASTFED INFANTS: PRELIMINARY RESULTS OF A PROSPECTIVE TRIAL

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Purpose of Study: The American Academy of Pediatrics (AAP) has recommended universal supplementation of breastfed infants with vitamin D (200 IU/day) from 2 months of age; this recommendation was recently increased to 400 IU/day from birth. However, there are few studies of such universal supplementation. We are therefore conducting a clinical trial to compare vitamin D supplementation with placebo control in breastfed children.

Methods Used: After obtaining approval from the Ochsner Institution Review Board (2006-186A) normal newborns (breast milk intake >50 percent of total) were randomized into three groups: no supplementation, 200 IU per day from 2 months, and 200 IU per day from birth. Blood samples and questioners were collected at birth, two, four, and six months of age.

Summary of Results: We have recruited 74 subjects, and 19 subjects have completed. Preliminary data indicates little benefit to supplementation - no patients in the study have developed rickets, and we saw only mild, transient increases in alkaline phosphatase in the placebo vs. control group. The only statistically significant change in alkaline phosphatase levels occurred at 2 months (Vit.D 93 $\pm$ 12, placebo 125 $\pm$ 10 IU/l, $p<0.05$), even though there was no statistically significant difference in 25-vitamin D levels at that time point (Vit.D 97 $\pm$ 18, placebo 62 $\pm$ 8 nmol/l, NS). Statistically significant differences in 25-vitamin D levels were observed at the 4 month time point (Vit.D 137 $\pm$ 37, placebo 63 $\pm$ 9 nmol/l, $p<0.05$), but by 6 months the 25-vitamin D levels in the placebo group had risen to those of the treatment groups (Vit.D 132 $\pm$ 29, placebo 117 $\pm$ 28 nmol/l, NS). While serum calcium did not differ between groups, phosphate rose and PTH fell in the treatment groups (vs. baseline and vs. placebo), consistent with known effects of vitamin D.

Conclusions: Our preliminary data did not show any benefit to supplementation. Our previous report on vitamin D supplementation increasing the risk of urinary tract infection (Katikaneni R, et al., Breast feeding does not protect against urinary tract infection in the first 3 months of life, but vitamin D supplementation increases the risk by 76%. Clinical Pediatrics, 2009) we have concerns about the current AAP recommendations for universal supplementation with vitamin D in breastfed infants.

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TREATMENT OF CHEMOTHERAPY-INDUCED OSTEOPOROSIS AND ALOPECIA WITH A NOVEL FUSION PROTEIN IN YOUNG MICE

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Purpose of Study: Osteoporosis and hair loss are two major side-effects of chemotherapy. So far, no satisfactory strategy for preventing or treating chemotherapy-induced alopecia is available. Therefore we designed a study to see if we can treat or prevent the hair loss as well as bone loss caused by chemotherapy in young mice.

Methods Used: To test the effects of PTH-CBD on osteoporosis and alopecia in mice treated with cyclophosphamide (CYP). 8-week old female C57BL/6J mice were treated with CYP (150 mg/kg three times) every two weeks for a period of six weeks.

Summary of Results: Treatment with a single dose of PTH-CBD (320 mcg/kg) at this time resulted in marked increased bone mineral density (22 percent), and the thinning/graying of the hair was reversed after 21 days. The hair changes persisted to the time of sacrifice (9 months after PTH-CBD administration). Histological examination of the skin showed increased number and depth of hair follicles in the subcutaneous tissues in the PTH-CBD treated animals. In a separate study, 3-month old C57BL/6J mice were divided into 3 groups, one receiving CYP alone (CYP), one receiving PTH-CBD prior to CYP administration (PTH-CBD/CYP), and once receiving no treatment (CTRL). Within 8 weeks, PTH-CBD/CYP mice showed higher bone mineral density and higher levels of alkaline phosphatase than did CYP mice. CTRL mice showed similar values to PTH-CBD/CYP mice. BMD in the CTRL mice peaked at age 5 months, while BMD in CYP mice peaked to a similar level at age 6 months. BMD in PTH-CBD/CYP mice exceed those peak values and are still increasing at age 9 months. Regarding effects on alopecia, CYP mice began to show thinning and graying of the hair at age 9 months (6 months after therapy), while PTH-CBD/CYP mice and CTRL mice have normal hair.

Conclusions: It thus appears that our new fusion peptide, PTH-CBD, can prevent or reverse chemotherapy-induced osteoporosis and alopecia in mice,

and may ultimately serve as a therapy to treat osteoporosis and hair loss in patients undergoing chemotherapy.

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FRAX FAILS TO CHANGE PRESCRIBING BEHAVIOR DESPITE INCREASED RECOMMENDATION TO TREAT

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Purpose of Study: Prevention of fractures in osteoporotic patients using FDA approved drugs is desirable to decrease morbidity, mortality, and health care costs. Introduction of the WHO FRAX tool was expected to enhance physician decisions on treatment by capturing high risk patients that would have been otherwise missed using only bone density T scores. We sought to determine compliance with FRAX and its impact on prescribing behavior in an outpatient setting.

Methods Used: We retrospectively reviewed compliance of clinicians to FRAX recommendations in a group of patients that underwent bone densitometry 1 year before and 1 year after the introduction of FRAX recommendations in bone density reports. We focused on osteopenic patients (DXA -1.0>T>-2.5) since this group would be most influenced by FRAX. Exclusions: <50 years old, known osteoporosis. Demographic information, provider type, DXA/FRAX results and the decision to prescribe an FDA approved drug within 6 months of DXA were captured. Data was analyzed using chi square.

Summary of Results: 970 charts were reviewed and 268 met inclusion criteria (102 pre-FRAX, 166 FRAX). FRAX recommended treating 32% (53/166) of patients with osteopenia who might not have been treated using DXA alone. Of these, only 30.2% (16/53) were treated and 69.8% (37/53) were not treated despite FRAX recommendation to treat. 9.7% (11/113) of FRAX patients were treated contrary to FRAX recommendation not to treat. In the pre-FRAX group, 8.9% (9/101) were treated contrary to DXA recommendation. Overall, more patients were treated in the FRAX group (27/166; 16.3%) compared to the pre-FRAX group (9/102; 8.8%) but the difference was only partly attributable to FRAX recommendations. There was a significant relationship between the type of tool used and the compliance of clinicians to its recommendations (P<0.0001). Compliance to DXA recommendation was 91.2% while compliance to FRAX recommendation was 71.1%.

Conclusions: Despite evidence supporting the benefit of using the FRAX tool, we found that (1) physicians had poor compliance with FRAX, (2) prescriptions were increased with FRAX but was only partly related to the recommendation, (3) FRAX had no benefit to patients since it was mostly ignored. There is therefore a need for increased awareness and use of FRAX in decision making.

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TELEMEDICINE IN DIABETES CARE: LESSONS FROM THE ADDRESSING DIABETES IN TENNESSEE (ADT) PROJECT

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Purpose of Study: The prevalence of diabetes in Tennessee has risen over 2-fold between 1997 and 2007 from 5.0 to 11.0%; with estimated diabetes related mortality of 30 per 100,000. Rural communities bear a high burden of diabetes due to rising prevalence and shortage of physicians. Application of telehealth may improve diabetes care and outcome. ADT aimed to assess the impact of a telehealth-based diabetes management program on diabetes care in rural areas with high diabetes-related mortality.

Methods Used: Diabetic patients aged ≥18 years, with A1c ≥8.0% were recruited and given diabetes self management education (DSME) by a certified diabetes educator via video-conference every 3 months. At the end of each class, a question and answer session on diabetes management was conducted by an endocrinologist; who also provided individualized endocrine consultation as needed, if it was approved by the primary care provider. Data were collected on outcome measures, e.g., A1c, BP and cholesterol levels. After 9 months, patients were contacted to elicit their level of participation and diabetes control.

Summary of Results: We recruited 42 patients (66% females, mean age-55.6 ± 10.0 years). A1c and total cholesterol were reduced significantly after intervention (10.0 ± 1.6% vs 8.3 ± 1.4, P <0.001) and (187 ± 43.4 vs 175.8 ± 41.7, p< 0.05) respectively. BP, LDL, HDL and TG were not significantly different. All patients believed the program was cost effective and would use

it again and 97% of them stated it was useful in developing a treatment plan, which resulted in better diabetes control. However, not all patients attended all classes. Compared to patients who attended <50% of the classes, those who attended >50% were older (54.0 ± 7.5 vs 62.4 ± 8.4, yrs P<0.01) and liked the group format of the classes better (91% vs 53%, P <0.05), but glycemic control was significantly improved in both groups (p<0.05).

Conclusions: A telehealth-based diabetes management program incorporating DSME and individualized consultation was an acceptable and effective means of improving diabetes care in rural areas with high diabetes-related mortality. Older patients may need more classes than younger subjects. Hence future studies should take into cognizance participants' age and preferred class format.

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MOLECULAR ABNORMALITIES IN CD4 T-LYMPHOCYTES FROM NOD MICE: THE PREINSULINITIS STAGE

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Purpose of Study: CD4 T-lymphocytes play a prominent role in induction of autoimmunity in DM1 in both humans and Non-Obese Diabetic (NOD) mice. To gain a deeper insight into the molecular events that lead to initiation of DM1, we evaluated mRNA levels in CD4 T-lymphocytes of NOD mice at age 2-4 weeks (before the appearance of insulinitis).

Methods Used: Total RNA was extracted from spleen CD4 T-lymphocytes of NOD mice and two control strains: NOR and C57BL/6 at 2, 3 and 4 weeks of age. mRNA levels were assayed on Affymetrix expression arrays interrogating ~39,000 mouse genes.

Summary of Results: Analysis by 1-way-ANOVA (at Benjamin-Hochberg adjusted p<0.005 level) identified 311, 624, and 581 probesets (genes) with highly significant expression differences between strains at 2, 3 and 4 weeks, respectively. Hierarchical clustering of these gene lists revealed 58, 115, and 65 genes, respectively, were differentially expressed in NOD compared to both control strains (41 lower, 17 higher in NOD at 2 weeks; 83 lower, 32 higher at 3 weeks; and 56 lower, 9 higher at 4 weeks). We subjected the 3 lists (58, 115, and 65 genes) to Ingenuity Pathway analysis. Of 15 genes ranked as the most central in the generated networks, 7 (HNF4A, TP53, BCL2L1, IFNG, IL4, IL15, and prostaglandin E2) were common to all 3 ages. IL6 was central only in networks of 2 and 4 week old mice. Genes specifically central to networks of each age group included: MYC, JUN and HRAS at 2 weeks; TNF, NFKB, p38MAPK, and TGFBI at 3 weeks; and Interferon alpha, IL12 and STAT4 at 4 weeks.

Conclusions: Central genes common to networks of all 3 ages suggest basic abnormalities in apoptosis/cellular proliferation, Th1-Th2 differentiation, cytokine signaling, and inflammation. Genes specifically central to networks of each age group suggest that abnormalities in apoptosis/cellular proliferation predominate at 2 weeks of age while those in cellular activation and inflammation predominate at 3 weeks of age. Furthermore, abnormalities in the innate immune response and its link to adaptive immunity predominate at 4 weeks of age. In summary, the study identified basic (genetic) and age-specific molecular abnormalities in CD4 T-lymphocytes in the preinsulinitis stage of DM1.

Gastroenterology and Clinical Nutrition I

Concurrent Session

2:00 PM

Friday, February 26, 2010

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GENE EXPRESSION PROFILE OF INFLAMMATORY MEDIATORS AND EXTRACELLULAR MATRIX AND ADHESION MOLECULES IN EOSINOPHILIC ESOPHAGITIS

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Purpose of Study: Eosinophilic esophagitis (EoE) is a rapidly expanding disease of the esophagus encountered in children and adults, so that in gastroenterology this decade was called the decade of EoE. It is an inflammation of the esophagus that does not respond to acid suppression therapy. EoE causes massive eosinophil infiltration, remodeling of the esophageal epithelium, severe hyperplasia, furrows and thin crepe-like mucosa.

Methods Used: To study the factors involved in esophageal tissue damage and remodeling, we used real-time qPCR to study the expression of two panels of genes in pinch biopsies obtained during routine endoscopy procedures in EoE and normal patients (NL). The first panel contains 84 genes involved in the inflammatory response. The second panel contains 84 genes playing a role in extracellular matrix (ECM) structure, cell-to-cell communications and cell-matrix adhesion. We also used cytokines and growth factors protein arrays as well as immunohistochemistry (IHC) to determine & localize specific proteins involved in the above pathways.

Summary of Results: Our data show that eotaxin 3 is very prominently upregulated (~200 folds) as well as its receptor CCR3 (~23 folds). Interleukins (IL), IL13 and IL5 are upregulated by 10 and 4 folds respectively. These data are consistent with previously reported observations. In the ECM gene panel, CD44 and CD54 (ICAM1), both hyaluronan binding molecules, and genes for ECM proteases (ADAMTS1 and MMP14) are upregulated significantly. Collagen genes (COL6A1 and COL15A1) are upregulated (~3X), whereas COL14A1 is downregulated (~2X). IHC experiments using an antibody to CD44 showed more intense staining in EoE biopsies than in NL. A label-based cytokine and growth factors antibody array showed an increase in epidermal growth factor (EGF) and fibroblast growth factor (FGF7) in EoE biopsies.

Conclusions: We have identified a number of novel genes whose expression is altered in EoE. Their role in inflammation and esophageal tissue damage could reveal the mechanisms of remodeling observed in the disease.

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ENTERAL SUPPLEMENTATION OF AMNIOTIC FLUID-BORNE HEPATOCYTE GROWTH FACTOR DECREASES NECROTIZING ENTEROCOLITIS IN RAT PUPS

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Purpose of Study: The fetus swallows amniotic fluid (AF), which contains several bioactive molecules that promote gut mucosal development in the fetus. This exposure to AF-borne factors is interrupted following premature birth, which may increase susceptibility of the immature gut to NEC. We investigated whether supplementation of formula feeds with AF can protect rat pups from NEC-like injury.

Methods Used: We used an established hypoxia & hypothermia model of NEC to study 80 rat pups in two groups (experimental group fed RMS +30% AF, controls fed only RMS; both received hypothermia and hypoxia q12 hrs). Animals were compared for NEC-like injury at demise or after euthanasia at 96 hrs. Twenty-nine different cytokines and GFs were measured in AF from d18 -19 pregnant rats (n=9) using a multiplex bead assay/ELISA. We next used IEC6 intestinal epithelial cells (IECs) to investigate the effect of AF on IEC migration (monolayer scratch assay), proliferation (BrDU incorporation), and protection against TNF- α /cycloheximide (CHI)-mediated cellular injury (XTT assay) in vitro. We then repeated these experiments with rHGF and with AF+ neutralizing anti-HGF antibody (10 g/mL).

Summary of Results: AF supplementation reduced the frequency (47% vs. 65%; $p<0.05$) and severity (grade 0.8 vs. 1.63; $p<0.05$) of NEC-like injury. In vitro, AF increased IEC6 cell migration (8.2+2.9 and 11+3.9 cells with 10% and 20% AF vs. 4.1+1.4 cells with media alone, $p<0.01$) and proliferation (BrDU incorporation measured as optical density: 0.993 + 0.03 and 1.358 + 0.07 with 10% and 20% AF vs. 0.752+0.02 with media alone; $p<0.001$). AF also significantly reduced TNF- α /CHI-mediated cell injury. The most abundant GFs/cytokines in AF were HGF (8953+805 pg/mL), IL1ra (1909+202.4 pg/mL), epidermal GF (190+26 pg/mL), and IL-8 (148.1+28.4 pg/mL). The protective effects of AF were partially recapitulated in vitro by rHGF and were also partially blocked by added anti-HGF antibody, thereby emphasizing the importance of HGF in mediating AF effects.

Conclusions: AF supplementation protects rodent pups against experimental NEC like mucosal injury, which is mediated, at least in part, by HGF. Further studies are underway to determine the role of HGF as a trophic supplement in formula feeds.

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BACTERIAL COLONIZATION DRIVES DEVELOPMENT OF GUT MUCOSAL MAST CELLS

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Purpose of Study: Gut mucosal mast cells (MMC)s serve a sentinel function by 'reporting' translocating bacteria to resident phagocytes and play a key role in mucosal inflammatory responses. Because MMCs share the myeloid lineage with macrophages, we hypothesized that MMC populations, like macrophages, develop in the fetal intestine as a function of gestational age.

Methods Used: c-kit⁺ intestinal MMCs were enumerated in human fetuses (22 $\pm$ 1.5 wks gestation), premature neonates (24 $\pm$ 1.2 wks gestation), and adults, and from E20 murine fetuses and germ-free (GF) and conventionally-reared (CR) mice at 3-4 and 10-12 wks of age. Expression of MMC chemokines was measured by qPCR/western blots/IHC. Mast cell chemotactic activity of gut epithelial-conditioned media (E-CMs) was measured in vitro using the EML cell line in a fluorescence-based assay.

Summary of Results: MMCs were infrequent in human fetal intestine (1.7 $\pm$ 0.2/villus) but were readily seen in premature neonates (4.7 $\pm$ 0.4/villus; $p<0.05$). MMC counts in adults (5.3 $\pm$ 0.6/villus) were not significantly higher than premature neonates. MMC counts were also low in E20 murine fetal intestine (0.2 $\pm$ 0.05/villus), thereby confirming the paucity of MMCs prior to birth. Therefore, we next investigated the role of bacterial flora in MMC development: GF mice had only 0.1 $\pm$ 0.7 and 1.9 $\pm$ 0.3 MMCs/villus at 4 and 10 wks of age, compared to 9.1 $\pm$ 0.7 and 10.5 $\pm$ 0.7 MMCs/villus in CR animals. We next colonized some GF mice with a non-pathogenic, well-defined flora (altered Schaedler's flora, ASF), which increased MMC counts to 5.6 $\pm$ 0.4/villus and 5.8 $\pm$ 0.4/villus at 4 and 10 wks of age. Because MMCs are incapable of clonal expansion, we used a qPCR array to measure expression of chemokines that recruit MMC precursors and identified CXCL12; E-CMs derived from CR and ASF intestine recruited EML cells in vitro, and this effect was blocked by anti-CXCL12 antibodies.

Conclusions: (1) Intestinal MMC development occurs not in utero but postnatally as a response to bacterial colonization; (2) CXCL12 recruits MMC precursors to the intestine; (3) MMCs increased in ASF mice but did not reach CR levels, indicating that luminal bacteria may display differences in their potency for recruitment of mast cells precursors to the lamina propria.

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TNFR1 SIGNALING PROMOTES COLON EPITHELIAL CELL REPAIR FOLLOWING INJURY AND PROTECTS AGAINST PROGRESSION TO INFLAMMATION-ASSOCIATED CARCINOGENESIS

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Purpose of Study: Inflammatory bowel disease (IBD) is a predisposing condition for colitis-associated carcinoma (CAC). Tumor necrosis factor (TNF) is a pro-inflammatory cytokine active in the pathogenesis of IBD and found in the context of numerous cancers. TNF receptor 1 (R1) has been shown to govern apoptosis and cell survival. Given the associations of IBD, cancer and TNF, we sought to understand the role of TNFR1 in experimental colitis and the progression to CAC.

Methods Used: We used the azoxymethane/dextran sodium sulfate mouse model of recurrent colitis that mimics IBD and variably leads to tumor formation in WT, TNFR1- and TNF-deficient animals. Outcomes measured included weight, hematochezia and colon length, mucosal damage and tumor grade. To characterize alterations in global gene expression over the course of treatment and the differences between WT and TNFR1 knockouts we performed microarray analysis at 3 timepoints. Expression of differentially expressed genes was confirmed using semi-quantitative PCR.

Summary of Results: Loss of TNFR1 but not of TNF resulted in worse outcomes: poor growth; protracted hematochezia; increased histologic inflammation; higher rates of more invasive carcinoma. By contrast, mice lacking TNF but with intact TNFR1 were relatively spared. Among the genes significantly upregulated in treated TNFR1- animals are those coding for TNF, Wnt inhibitory factor 1, and lymphotoxin. Moreover, in WT animals the remarkable differences between treated and untreated groups are manifest in pathways of inflammation and modulation of apoptosis. By contrast treated TNFR1- mice had alterations in pathways controlling DNA repair.

Conclusions: Absence of TNFR1 signaling aggravates epithelial cell injury, and loss corresponds with accelerated in vivo neoplastic transformation. The receptor is important in regulating the inflammatory response and apoptosis, and its loss is associated with deranged DNA repair pathways. These results confirm the importance of TNF in the linked processes of inflammation and carcinogenesis and highlight the critical function of TNFR1 in the response to injury and protection from malignant disease.

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OBESITY- A REAL MEDICAL CHALLENGE WITHOUT A REAL SOLUTION. CAN PERIPHERAL NERVE STIMULATION OF THE OCCIPITAL REGION HELP TO LOSE WEIGHT?

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Purpose of Study: During this therapy with Peripheral Nerve Stimulation (PNS) of the occipital region (C1-C2) for chronic headaches/migraines, some patients have noticed reduction of appetite. C1-C2 neuromodulation being reversible and less invasive surgical intervention could bring a new approach to treat obesity. Aim was to investigate the change in patients weight by using C1-C2 PNS in subjects with BMI ≥ 40 .

Methods Used: Five morbidly obese subjects were subcutaneously implanted with two temporary, horizontally placed leads [Octrode[®], ANS, Plano, TX] and an external stimulator [MTS[®], ANS, Plano, TX]. After 8 weeks of therapy, if at least a 4% reduction in weight was observed, leads and MTS were replaced with a permanent implantable pulse generator IPG [Eon[®], ANS, Plano, TX]. There were 6 different sets of continuous or cycling PNS parameters available to choose the best setting, based on satisfaction in controlling appetite. Patient status was monitored with clinical and QOL questionnaires. A Slow Nutrient Drink (SND) Test was performed at baseline and at F/U visits. No specific dietary or lifestyle modifications were mandated.

Summary of Results: Four subjects (3F, 1M) mean age 46 (31–56) mean weight 323.9lbs (228–461.8), mean BMI 49.2 (40–62.6) were implanted with temporary and later on permanent leads and IPG. One of the originally implanted subjects developed a local skin infection, requiring surgical revision and subsequently removal of the system. After a total 18 months of active stimulation, subjects lost on average 47 lbs (21.4kg) (14.4% of TBW) (range 2–121.8lbs) and BMI fell by a mean of 13% (range 1–26%). SND Test showed 12% reduction of Ensure intake, with 1003ml at baseline and 816ml at 12 months. It took on average 30.5min before PNS and 18min after C1-C2 stimulation to reach the maximal satiety (41% reduction). No unexpected device or study related SAEs were observed during this investigation.

Conclusions: Chronic C1-C2 neuromodulation can induce early satiety and accompanying weight lost. This pilot study of morbidly obese patients shows good safety and tolerability of PNS. More studies in a larger population will determine if this therapy is a valuable option in managing morbid obesity.

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MORBIDITY AND MORTALITY OF HEALTH CARE ASSOCIATED VERSES COMMUNITY ACQUIRED CLOSTRIDIUM DIFFICILE COLITIS - DO THEIR OUTCOMES DIFFER?

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Purpose of Study: We compared morbidity and mortality in health care associated (HCA) Clostridium difficile colitis (CDC) to that of community acquired (CA) CDC.

Methods Used: We retrospectively studied the occurrence of CDC over 12 months in an inner city urban community teaching hospital. Sixty three patients were diagnosed with CDC by fecal toxin assays. Patients with no prior history of hospital admission or antibiotic exposure in the past 3 months were considered to be CA-CDC. Patients with recent hospital admission, those who acquired infection in the hospital or who were admitted from a long term facility were considered HCA-CDC.

Of the 63 patients, 50 (79%) HCA-CDC. Chi square and Wilcoxon sum rank tests were used to compare factors associated with morbidity and mortality, and independent risk factors were further analyzed by multiple logistic regression.

Summary of Results: Number of co-morbidities, low albumin, African American ethnicity, sepsis, intravenous vancomycin use and treatment in ICU/CCU were significant predictors for both morbidity and mortality. Female gender, chronic kidney disease (CKD), proton pump inhibitor use (PPI), number of antibiotics used and need for colonoscopy were also significantly associated with morbidity. Independent significant prognostic factors for complications like ileus, pseudo membranous colitis and toxic megacolon were intravenous imipenem use [$p < 0.05$, OR-41.7], female

gender [$p < 0.05$, OR- 40.3], PPI users [$p < 0.05$, OR -29.4], CKD [$p < 0.05$, OR-13.9]. There was a significant 18% decrease in risk for complications for each mg/dl increase in albumin. Complications themselves [$p = 0.002$ - complicated course VS. non - complicated course, OR-58.8] together with treatment in ICU/CCU [$p = 0.04$ - treatment in ICU/CCU VS. regular floor, OR -13.5] were independent significant prognostic factors for mortality.

HCA versus CA-CDC patients did not differ significantly in complications. For all cause mortality, there were no deaths among the 13 patients (0%) with CA-CDC, but there were 9 deaths among the 50 patients with HCA-CDC ($P = 0.18$).

Conclusions: Although numbers did not reach statistical significance, there were no deaths in CA-CDC but 18% of patients with HCA-CDC died.

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ENDOSCOPIC PAPILLECTOMY OF AMPULLARY ADENOMAS: COMPLICATIONS AND OUTCOMES

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Purpose of Study: Ampullary adenomas have the potential for natural progression from a benign adenoma to more malignant forms. Endoscopic papillectomy with curative intent has gained credibility as a safe and effective procedure rather than surgery. This study was designed to assess the outcomes of endoscopic papillectomy for ampullary neoplasms at a single center.

Methods Used: Between May 1996 and August 2009, 47 patients were diagnosed with ampullary adenomas by endoscopic retrograde cholangiopancreatography (ERCP). 38 endoscopic papillectomies (ESP), 4 transduodenal resections (TDR), and 2 pancreatoduodenectomies (PD) were performed. Tumors in the remaining 3 patients were not amenable to safe endoscopic or surgical resection. ESP was performed by snare excision and electrocautery. Patients were followed up prospectively for complications and follow up endoscopy and biopsy recommended.

Summary of Results: Among the 47 patients (20 males and 27 females; mean age, 56.1 $\pm$ 14.1 years; range, 22–85 years) assessed, 8 had a final diagnosis of high-grade dysplasia (HGD), 32 with low-grade dysplasia (LGD), 4 with adenocarcinoma, 2 with adenomyoma, and 1 with a gastrointestinal stromal tumor (GIST), based on the Vienna classification system. Results showed a direct relationship between HGD occurrence and larger tumor sizes (range, 8–40 mm; $p = 0.011$). Tumor size by EUS was determined as 1.55 $\pm$ 0.71 in LGD, 2.66 $\pm$ 1.22 in HGD, and 3.75 $\pm$ 1.77 in cancer. Mean follow-up time was 16.5 $\pm$ 19.7 months (range, 0–82.5 months). Endoscopic complications (12.8%) occurred for 6 patients: 2 patients with bleeding, 3 patients with mild postpapillectomy pancreatitis, and one patient with infection.

Of the four patients with LGD and two patients with HGD developing recurrence, none developed tumors progressing from LGD to HGD or HGD to cancer. Kaplan-Meier analysis showed no significant differences in recurrence between the HGD and LGD groups ($\chi^2 = 2.2421$, df=1, p -value=0.1343).

Conclusions: Endoscopic papillectomy is a safe and effective treatment for benign ampullary neoplasms without significant mucosal invasion and represents an alternative to surgical therapy. A thorough evaluation of clinicopathologic features, notably degree of tumor extension, is necessary for accurate determination of treatment modality.

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WIDE VARIATION IN NURSING PRACTICE OF CHECKING GASTRIC RESIDUAL VOLUMES BASED ON OLD DOGMAS: CALL FOR A UNIFORM EVIDENCE BASED PROTOCOL

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Purpose of Study: It is a common practice to check gastric residual volumes (GRV) in tube feeding patients to monitor for any impairment of gastric emptying in order to reduce the risk of aspiration pneumonia. Most hospitals and health care providers follow a variety of individualized practices for checking GRV in tube fed patients. As part of systems improvement project, we examined the nursing practice of checking GRV in our hospital.

Methods Used: We conducted a survey of nurses in our hospital using a standardized questionnaire. A random sample of nurses from the medical/

surgical floors as well as ICU participated in the survey; none refused. The questionnaire included questions about practice of checking GRV including time spent and adherence to physician orders.

Summary of Results: 73% of nurses checked GRV q4hr, 15% q6hr and 10% q shift. 21 percent of the nurses reported that MDs write GRV orders 21% of the time. On the other hand, only 10% reported that GRV orders are written 100% of the time. Yet, all of them of the nurses checked GRV.

63% of the nurses held the tube feedings at 150ml GRV while 42% of them used a 200ml threshold. Although 94% of the nurses answered “yes” to holding tube feeds for “high GRV,” only 68% reported this to the physicians.

42% of nurses believed that checking GRV, calling MDs and call backs about high residuals consumed <5% of their time, whereas 26% of nurses reported 10–20%, and 5% of nurses believed the time consumed to be felt 25% of their duty time.

Conclusions: We observed a wide variation in practice of management of GRV in a single hospital setting. This time consuming practice in asymptomatic patients is inconsistent with the lack of predictive value for GRV for predicting risk for aspiration pneumonia. On the other hand, this leads to holding tube feeds, majority of which are avoidable and potentially affect patient outcomes. This calls for the use of standardized evidence based protocol to check tube feeds and this should be an integral part of hospital policy. We would like to share our proposed hospital GRV check protocol during presentation.

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GASTRIC HYPERPLASTIC POLYP PRESENTING AS IRON DEFICIENCY ANEMIA

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Case Report: BACKGROUND: A diverse array of polyps and polypoid lesions may be found in the stomach. The most common is the fundic gland polyp. The majority of gastric polyps are asymptomatic. However, large polyps can erode and have chronic bleeding from the erosion site which produces iron deficiency anemia. We present a case was referred for evaluation of iron deficiency anemia who was found to have a large gastric antral polyp. Polypectomy cured her anemia without further intervention.

OBSERVATION: A 70 year old woman was referred for endosonographic evaluation of a large gastric antral polypoid lesion found on upper endoscopy done for evaluation of iron deficiency anemia. Her hemoglobin was 9.9 g% (Normal 12–14g%), MCV was 79 fL (normal 80–95 fL). The initial pathology from the referral site showed a hamartomatous polyp and the concern was an exclusion of invasiveness which will indicate a malignant behavior of the polypoid lesion. The patient had a complaint of general weakness. The EUS showed a well-defined, hyperechoic lobulated mass, 42mm by 12 mm in the antrum of the stomach arising from the mucosal layer and not extending to the deeper layers. An EGD was subsequently done. It showed a large polypoid lesion as described above with small erosion at the top. The lesion had a broad based pedicle. The lesion was removed using a hot snare piecemeal technique and the excision site was clipped. The surrounding gastric mucosa was biopsied. The large polyp pathology showed a thick, mostly foveolar epithelium with a moderate infiltrate of plasma cells and lymphocytes with no signet ring cells or gland fusion with smooth muscle core, consistent with a hyperplastic polyp. The gastric mucosa showed changes of common reactive gastropathy with mild chronic inflammation, no *Helicobacter pylori* was identified. Upon follow up, the patient was asymptomatic. Her follow up hemoglobin increased to 12.1 g% without supplemental iron therapy.

DISCUSSION: Gastric hyperplastic polyps are not uncommon. They may present as iron deficiency anemia or gastric outlet obstruction or may be asymptomatic. Careful gastric mapping to check for *H.pylori*, intestinal metaplasia and gastric atrophy should be sought and individualized surveillance plans should be implemented for these high risk conditions.

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FROSTIER SYNDROME; A RARE CAUSE OF DYSPHAGIA

WM. Frandah, H. AlTamimi *TTUHSC, Lubbock, TX.*

Case Report: BACKGROUND: Diffuse Idiopathic Skeletal Hyperostosis (DISH) is a common condition in the aging spine. DISH is associated with large anterior osteophyte of the cervical spine, which occasionally causes complications by compressing adjoining structures. We present a patient who presented to the clinic with a rare cause of dysphagia. We discuss the clinical presentation, mechanism of dysphagia and potential therapies for such a condition.

OBSERVATION: A 49 year old man presented to the gastroenterology clinic with solid food dysphagia of 2 years duration. He described his symptom as “food getting stuck in his throat” even after careful chewing and swallowing with partial facilitation when drinking liquids. Patient had history of heartburn for two years, but no history of odynophagia, hoarseness of voice, loss of appetite or loss of weight. He has a 45 pack-year history of cigarette smoking and drinks a six pack of beer per week for thirty years. No significant past medical or surgical history. On physical examination, he was an average built man with no palpable cervical or supraclavicular lymph nodes. Cardiopulmonary and abdominal examination was normal. Neurologic examination was also intact. Initial evaluation included an esophagogram which showed a filling defect immediately below the hypopharynx with transient filling defect in the mid-thoracic esophagus. EGD revealed normal esophagus with mild gastritis and mild duodenitis. Subsequently he underwent CT scan of the neck with and without cervical spine reconstruction which revealed an extremely large anterior bridging osteophyte with large thick flowing anterior syndesmophyte extending from C3 through C5 with calcification. A diagnosis of Diffuse Idiopathic Skeletal hyperostosis was made and patient was referred to a neurosurgeon. He had osteophyctectomy with uneventful recovery and substantial recovery of his dysphagia.

DISCUSSION: Frostier syndrome, even though rare, should be considered in the differential diagnosis of patients with a complaint of dysphagia.

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A CASE OF TETANY: A PANDORA'S BOX

KP. Patra, W. Wells *LSUHSC, Shreveport, LA.*

Case Report: A 12 year old boy presented with a 2 week history of leg cramps and one day history of carpal spasms. He also reported a one month history of nausea, epigastric pain and recurrent non-bloody diarrhea. There was a history of involuntary weight loss of 10 pounds over 2 months. Physical examination revealed positive Trousseau sign while Chvostek sign was negative. The remainder of physical findings were normal. Laboratory investigations showed hypocalcemia (total =5.3 mg/dl, ionized =0.7mmol/l, corrected calcium=6.1 mg/dl) and serum albumin (3 g/dl). Serum magnesium, bilirubin, liver enzymes, amylase, lipase and blood glucose were normal. Hemoglobin was 9.3 g/dl, white blood cells 9900/mm³, platelets 471,000/mm³ and ESR 46 mm/h. There was microcytic hypochromic anemia and the iron studies were suggestive of iron deficiency anemia. Serum 25OH vitamin D was decreased and serum parathyroid hormone was normal. Because of the abdomen pain, a CT abdomen was done which showed thickening of terminal ileum. Endoscopy revealed hypertrophied mucosa at the greater curvature of stomach, rectosigmoid junction and distal splenic flexure. Biopsies from same sites yielded numerous eosinophils (15/hpf). It was negative for *H.pylori* and there was no cryptitis or abscesses. Serial stool analyses for intestinal parasites were negative. Serum IgE was normal and radioimmune absorption studies for a panel of food allergens were negative. Work up for celiac disease was negative. The IBD serology7 panel was strongly indicative of Crohn disease (CD). He was discharged home on Balsalazide, calcium, vitamin D and prednisolone. Follow up visits showed resolution of symptoms, weight gain, normal blood counts and serum chemistries. This case brings out that high index of suspicion is required as CD can have protean manifestations. Perturbation in calcium homeostasis is a well-known albeit late feature in CD. This case is unique as tetany was the initial presentation. CD can be a diagnostic conundrum as often endoscopy and biopsy do not yield hallmark features. The constellation of clinical findings, ancillary laboratory studies, imaging and serologic markers can corroborate the diagnosis. Gastrointestinal eosinophilia can be a sole histologic finding in CD.

Hematology and Oncology I Concurrent Session

2:00 PM

Friday, February 26, 2010

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USING RADIOGENOMICS TO PREDICT RESPONSE OF LUNG CANCER TO RADIATION THERAPY

MH. Bell^{1,3}, A. Das¹, M. Peyton¹, Y. Xie¹, L. Girard¹, M. Story², C. Nirodi², J. Minna¹ ¹UT Southwestern Medical Center, Dallas, TX; ²UT Southwestern Medical Center, Dallas, TX and ³University of South Alabama College of Medicine, Mobile, AL.

Purpose of Study: Specific aims are to develop tumor mRNA and protein expression signatures predicting response to XRT before a patient is treated and to integrate this with signatures predicting response to chemotherapy (CTX) to ultimately facilitate selection of the best CTX regimen, XRT, and combined CTX + XRT for each individual patient.

Methods Used: We determined the XRT response phenotypes for a panel (up to 50) non-small cell lung cancers (NSCLCs) by performing radiation survival curves using clonogenic assays to determine the surviving fraction at 2 Gy (SF2). These values are integrated with our genome wide mRNA expression profiles on these same tumor lines with biostatistical approaches to develop mRNA expression signatures associated with sensitivity and resistance to radiation.

Summary of Results: Available SF2 values in NSCLCs are distributed over a range from 0.06 to 0.91. We also determined the repair kinetics of XRT induced DNA double strand breaks (DSBs) monitored by the disappearance of gH2AX and 53BP1 foci (determined by immunofluorescent staining with specific antibodies and scoring fluorescent foci). A striking correlation was found with increased radiosensitivity for NSCLC containing an EGFR oncogenic mutation and these tumor lines exhibited a deficiency in DNA DSB repair (see also *Das Can Res* 67:5267, 2007). Amundson et al., (*Can Res*, 68:415, 2008) recently reported a mRNA signature predictive of response to XRT in the NCI-60 panel of tumor cell lines. However, when we applied this signature to our mRNA array data we observed that their signature predicted that SCLC would be resistant to XRT which our previous studies and clinical experience disagree with their findings.

Conclusions: NSCLCs display strikingly different radiation response phenotypes reflected in the corresponding SF2 values that will allow us to develop mRNA signatures predicting response to XRT. Signatures developed by other investigators do not predict for lung cancer XRT response. Radioresistant cell lines are more proficient in repairing the radiation-induced DSBs but radiosensitive cell lines show delayed repair kinetics and retain 30% of DSBs even 24 hr post irradiation.

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INDUCTION OF CANCER CELL DEATH BY GENOMIC QUADRUPLIX-FORMING DNA SEQUENCES

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Purpose of Study: Four stranded quadruplex-forming DNA sequences occur naturally in telomeres and in the promoters of many eukaryotic genes. Although the mechanism of action is not clear, random quadruplex-forming DNA sequences have been shown to selectively kill cancer cells. One such sequence, AS1411, is currently in Phase II studies. In order to characterize the potential growth inhibitory effects of genomic quadruplex-forming sequences, we have characterized the effects of the c-myc promoter quadruplex-forming sequence (Pu27) and the Bcl-2 promoter quadruplex-forming sequence (Bcl-2q).

Methods Used: U937 leukemia cells were treated for increasing times with Pu27 and Bcl-2q at 5 μ M and 10 μ M concentrations. In selected experiments, the oligonucleotide-containing medium was removed after varying times and the cells were allowed to continue to grow in nonoligonucleotide-containing medium. Cell cycle arrest was characterized using flow cytometry.

Summary of Results: The c-myc quadruplex-forming sequence (Pu27) has been shown to play an important role in regulation of c-myc expression. We have shown that Pu27 inhibits the growth of U937 cells in a concentration dependent manner. In contrast, MutPu27, a mutated Pu27 sequence which does not form quadruplex (as documented by circular dichroism analysis) has no growth inhibitory activity. Neither oligonucleotide inhibits the growth of nontransformed cells. The growth inhibition induced by Pu27 is accompanied by a striking decrease in c-myc expression. The effect of Pu27 appears to be irreversible after exposure times of 72 hours, or more. Pu27-induced cell death is preceded by S-phase arrest. Pu27 is quite stable in medium with a half-life in serum containing medium of greater than 24 hours. Studies with fluorescent Pu27 demonstrate that it is also quite stable intracellularly. Quite similar results were seen for cells treated with Bcl-2q. However, Bcl-2q appeared to be more growth inhibitory in cells in which Bcl-2 participates in transformation.

Conclusions: The genomic quadruplex-forming sequences, Pu27 and Bcl-2q, are selectively toxic to malignant cells. These results suggest that genomic quadruplex-forming sequences have considerable potential as a treatment for leukemia.

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CARDIAC HORMONES ELIMINATE SOME HUMAN SQUAMOUS LUNG CARCINOMAS IN ATHYMIC MICE

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Purpose of Study: Four cardiac hormones synthesized by the same gene, i.e., atrial natriuretic peptide, vessel dilator, long acting natriuretic peptide and kaliuretic peptide, have anticancer effects in vitro. The present investigation was designed to determine if they might have beneficial effects in vivo on human squamous cell lung carcinomas in athymic mice when treated for 28 days via subcutaneous pumps.

Methods Used: These cardiac hormones were infused subcutaneously for 28 days with weekly fresh hormones at 0.3 nM kg⁻¹ body weight in athymic mice bearing human squamous cell carcinomas. Tumor growth was followed using digital electronic Vernier calipers.

Summary of Results: Vessel dilator, atrial natriuretic peptide and kaliuretic peptide each eliminated 1 in 6 (17%) of the human squamous cell lung carcinomas. Long-acting natriuretic peptide, although it did not eliminate any of the human squamous cell lung carcinomas did decrease the volume of one carcinoma to only 2% (p<0.0001) of the untreated carcinomas. The squamous cell lung carcinomas that were not eliminated, with the exception of the one LANP-treated tumor that decreased to only 2% of the volume of the untreated cancers, grew rapidly but their growth velocity compared to controls decreased by 76%, 40%, 38% and 25% in the vessel dilator, atrial natriuretic peptide, kaliuretic peptide and long-acting natriuretic peptide groups respectively (p<0.05).

Conclusions: Three of four cardiac hormones synthesized by the atrial natriuretic peptide gene can eliminate human squamous cell lung carcinomas in athymic mice when treated subcutaneously for four weeks. The 4th cardiac hormones, i.e. long-acting natriuretic peptide, decreased the volume of one squamous cell lung carcinoma to 2% of that of untreated animals, suggesting that it, too, has beneficial effects on squamous cell lung cancers.

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MOLECULAR DISSECTION OF RHABDOMYOSARCOMA TUMORIGENESIS

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Purpose of Study: Rhabdomyosarcoma (RMS) is a tumor of skeletal muscle-type histogenesis and the most common pediatric soft tissue cancer. RMS is often caused by one of two chromosomal translocations, t(1;32)(q35;q14) or t(2;13)(p36;q14), that are RMS specific and diagnostic. Despite aggressive multimodal therapy, the 5-year survival rate of patients with advance-staged RMS remains less than 30 percent and has not improved in over two decades. We intend to genetically characterize the molecular underpinnings of RMS to find new potential drug targets for treatment.

Methods Used: Since PAX biology is structurally and functionally conserved (as is syncytial muscle development and structure), we have generated a new transgenic PAX-FKHR *Drosophila* model, which we have used to conduct a forward unbiased genetic screen to identify dominant modifiers of PAX-FKHR pathogenesis when expressed in growing muscle tissue. We also performed microarray analysis of fly PAX-FKHR tissue versus control tissue. We are now actively profiling genetic loci of interest for phenotypes in mammalian murine C2C12 myoblasts.

Summary of Results: After testing a subset of candidate genes identified in the screen, we have found that the genes identified as genetic modifiers of PAX-FKHR pathogenicity in the fly screen are indeed active in mammalian myoblast biology and PAX-FKHR pathobiology. These genes include loci normally involved in myogenesis as well as genes not previously correlated with mammalian skeletal muscle development or PAX biology. A more detailed description of our preliminary findings will be provided after determining whether the candidate genes are expressed and participate in RMS pathobiology.

Conclusions: Our results suggest that the PAX-FKHR *Drosophila* transgenic model and genetic screening are revealing previously unknown gene targets that will likely underlie RMS pathogenesis. The discovery of new genes

seminal to RMS pathobiology will be a valuable tool in the conceptual design of new therapies to target RMS and thus improve treatment.

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A METHOD TO PREDICT GEMCITABINE ASSOCIATED PLATELET TOXICITY

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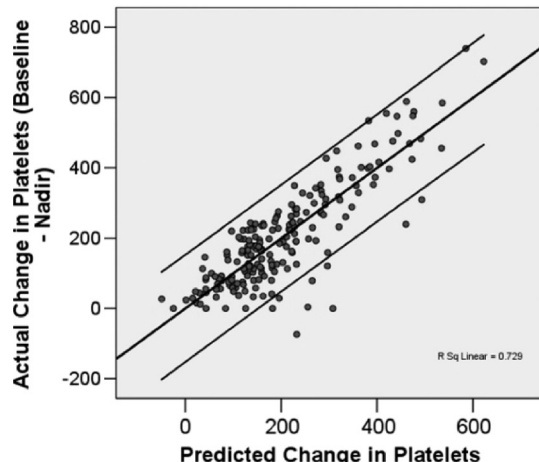
Purpose of Study: Chemotherapy agents have a very narrow therapeutic index and there is great deal of scrutiny in choosing the appropriate dose to treat cancer. Some oncologists reduce the doses of chemotherapy in obese patients to minimize toxicity. The body surface area has been adopted as a standard tool to calculate the dose for most chemotherapy agents and gemcitabine is not an exception. Thrombocytopenia is the dose limiting factor for use of gemcitabine. This study has delineated the risk factors involved in gemcitabine associated platelet toxicity and has proposed a formula to predict the severity of this side effect.

Methods Used: We retrospectively analyzed 200 pts who received gemcitabine treated for variety of cancers during a 11 year period in our cancer center. The percent of platelet decrease was chosen as a measure of toxicity. Using the analysis of covariance we evaluated the relation between platelet drop, race, sex and age of our pts. We used a linear regression model to demonstrate such a relationship between our variables.

Summary of Results: We found a significant relation between the percent of platelet drop and patient's race and sex. Our formula is: Predicted percent of platelet change = $[0.82 \times \text{PLT count at baseline} - 40.3 - 28.5 \times (\text{sex}) - 25.7 \times (\text{race})]$. Race=1 for African American and 0 for all other. Sex=1 for male and 0 for female. P value < 0.002 (Image 1).

Conclusions: We propose a formula to predict the percent of PLT drop in cancer pts treated with gemcitabine if the baseline PLT count, race and sex of the patients are known.

Predicted Change = $0.82 \times \text{Platelets (baseline)} - 40.3 - 28.5 \text{ (if male)} - 25.7 \text{ (if black)}$



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GERMLINE P53 MUTATION (LI-FRAUMENI SYNDROME) RESULTING IN THREE SEQUENTIAL MALIGNANCIES IN A CHILD

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Purpose of Study: Second malignant neoplasms (SMN) are important, but infrequent, complications of childhood cancer therapy. Third malignant neoplasms following successful treatment of two childhood cancers are very rare and suggest a cancer predisposition syndrome.

Methods Used: A retrospective case report is presented of a child with three sequential, malignancies treated at the same institution over an eight year period of time.

Summary of Results: The patient was diagnosed at 1 year of age with embryonal rhabdomyosarcoma (RMS) of the right thigh. He was treated with multiagent chemotherapy (vincristine, actinomycin, cyclophosphamide and topotecan), local radiation therapy to the right thigh (50 Gy) and delayed surgical resection. He was cured of his RMS. At age 7 years, he was diagnosed with localized osteosarcoma (OST) of his right femur. He received further chemotherapy (Adriamycin, cisplatin, methotrexate, ifosfamide and etoposide) and underwent resection of the tumor. Off therapy evaluation demonstrated no persistent or recurrent RMS or OST. Two months after completing therapy for the OST, he presented with leukemia cutis and pancytopenia and was diagnosed with myelodysplasia/acute myelogenous leukemia with monosomy 5. He failed to attain a remission with further chemotherapy and died of his disease three months after diagnosis of his third malignancy. Evaluation of his germline DNA identified a heterozygous c.743G> A mutation in the TP53 gene defining Li-Fraumeni Syndrome in this young child.

Conclusions: This report describes the extremely rare occurrence of three sequential malignancies arising in a child with germline mutation of the TP53 gene (Li-Fraumeni Syndrome). Treatment of rhabdomyosarcoma with radiation therapy resulted in osteogenic sarcoma arising in the radiation field. Treatment of osteogenic sarcoma with alkylating chemotherapy agents resulted in monosomy 5 associated myelodysplasia and acute myelogenous leukemia. The events of this case highlight the intersection of genetic risk factors and therapy decisions in childhood oncology that impact long term treatment outcome.

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MALE BREAST CANCER: A 20-YEAR SINGLE INSTITUTION EXPERIENCE

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Purpose of Study: Male breast cancer is a rare malignancy accounting for 0.5% of all male cancer deaths. It occurs at a male: female incidence of 1:70 in African Americans and 1:100 among Caucasians. It is associated with hereditary and genetic predisposing factors such as BRAC2 mutation, Jewish ancestry, Klinefelter syndrome among others. The majority of tumors are hormone receptor positive but negative for HER2neu.

Methods Used: An IRB exemption was obtained to review the charts from 1/1/1988 to 12/31/2008 of patients with male breast cancer treated at the Feist-Weiller Cancer Center. Sources include electronic medical records, medical records and the tumor registry. Demographic and clinical factors were evaluated and SAS software was used for statistical analysis.

Summary of Results: A total of 13 patients were identified from the search. The median age was 57.4 years with a standard deviation of 12.8 years. The median survival time was 53 months with a standard deviation of 46.8 months. Seven patients were Caucasian and six were African American. The distribution of patients by stage was as follows: Stage I (3 patients), stage II (5 patients), stage III (4 patients), stage IV (1 patient). Nine patients were ER positive, eight were PR positive. Only 5 patients have been tested for HER2neu and they were all negative. One patient of three tested for BRAC1 had a genetic variant of uncertain significance and the other two were negative. One patient of three tested for BRAC2 had a diagnosis favoring polymorphism and the other two were negative. Five out of six patients with recorded BMI were overweight and four of these were obese. Nine of thirteen patients were positive for lymph nodes. Eleven patients underwent either a mastectomy of modified radical mastectomy and nine patients received chemotherapy. Survival estimate of patients by stage was not significant (p=0.36) and neither was survival estimate by race (p=0.43). Sample size may be a limiting factor.

Conclusions: Male breast cancer is a rare disease that often presents in an advanced stage though in our population slightly more than half were diagnosed in early stage. There may be an association with BMI but sample size is a limiting factor for statistical analysis.

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MANAGEMENT OF EARLY STAGE DIFFUSE LARGE B CELL LYMPHOMA. A SINGLE CENTER EXPERIENCE

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Purpose of Study: Less than 20% of patients with Diffuse Large B Cell Lymphoma (DLBCL) present with Ann Arbor Stage I and II and are

defined as early stage or localized disease. Abbreviated chemotherapy (CHOP) followed by involved-field radiation therapy (IFRT) is considered standard therapy but CHOP alone is also considered an effective strategy. Rituximab (R) is an active agent and has shown improved survival in combination with chemotherapy in advanced disease. Purpose of this study was to look at clinical characteristics and therapeutic outcomes of patients with early stage DLBCL who were treated with CHOP-IFRT, RCHOP-IFRT, CHOP, RCHOP or surgery alone at our institution.

Methods Used: Retrospective chart review of all patients with Early stage Diffuse Large B Cell Lymphoma diagnosed and treated at LSUHSC Shreveport between 1998 and 2008.

Summary of Results: There were 41 cases of biopsy proven early stage DLBCL diagnosed at our institution, of which 19 (41%) were stage I. According to age adjusted international prognostic index (IPI), 6 (14.6%) were low risk, 31 (75.6%) intermediate risk and 4 (9.7%) were high risk for relapse. Treatment included CHOP-IFRT=10 (24%), RCHOP-IFRT=7 (17%), CHOP=5 (12%), RCHOP=19 (46%) and surgery alone in 1 patient. Follow-up ranged from 2–200 months. Complete remission was achieved in 38 (94%). There were only 9 (21%) relapses of which 2 had high risk IPI and rest had intermediate risk. Relapse according to treatment type was CHOP-IFRT=1, RCHOP-IFRT=2, CHOP=3 and RCHOP=3. Excluding 3 patients with primary refractory disease, time to late relapse ranged from 9.4 to 109 months. Median overall survival after 200 months was not reached.

Conclusions: Although, early stage DLBCL has excellent rates of complete remission and prolonged overall survival, early and late relapses can still occur. Rituximab was administered in 26 (63%) of patients and our high rate of CR (96%) could be attributed to it. Both, chemo-radiotherapy and chemotherapy alone appear to be highly efficacious therapies in this disease.

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REGULATION OF CC LIGAND 5/RANTES BY SECRETORY ACID SPHINGOMYELINASE - IMPLICATIONS FOR COMPARTMENTALIZATION OF CERAMIDE FORMATION

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Purpose of Study: The bioactive sphingolipid ceramide has been implicated in the regulation of various cellular processes, including apoptosis, infection, and inflammation. Acid sphingomyelinase (aSMase) promotes ceramide formation via hydrolysis of sphingomyelin, however the molecular mechanism(s) of aSMase regulation and its precise role in ceramide-mediated biological processes remain ill defined. Interestingly, the aSMase gene gives rise to two distinct enzymes - lysosomal sphingomyelinase (L-SMase), as well as a secretory sphingomyelinase (S-SMase) - via differential trafficking of a common protein precursor. The purpose of this study was to define the role of S-SMase in cellular ceramide signaling.

Methods Used: Enzyme activity assays, quantitative mass spectrometry for sphingolipidomic analysis, Western blotting, Cytokine Panel, ELISA, RT-PCR, indirect immunofluorescence.

Summary of Results: Previously, our lab identified serine 508 as a crucial residue for acute regulation of aSMase (Zeidan and Hannun, JBC 2007). Here, we show that a S508A mutant of aSMase exhibits defective constitutive and regulated secretion in response to inflammatory cytokines (TNF- α , IL-1 β), as well as impaired formation of C16-ceramide. Importantly, the S508A mutant retains L-SMase activity suggesting a specific role for S-SMase in C16-ceramide formation. A screen for downstream targets of S-SMase/Cer identified the chemokine CCL5 (formerly known as RANTES) as a candidate effector molecule. Regulation of CCL5 by aSMase was subsequently validated using both loss-of-function and gain-of-function models. Using mouse embryonic fibroblasts from neutral ceramidase (nCDase) and sphingosine kinase 1 (SK1) knockout mice, we also demonstrate that ceramide, and not one of its metabolites, is responsible for the signal to CCL5.

Conclusions: Taken together these data support a crucial role for Ser508 in the regulation of aSMase trafficking and function, and identify a novel role for S-SMase in cellular ceramide metabolism and chemokine elaboration.

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SMALL CELL LUNG CANCER: TIME TO DIAGNOSIS AND TREATMENT

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Purpose of Study: Small cell lung cancer (SCLC) is the most rapidly progressive of the bronchogenic carcinomas, with a doubling time of 30 to 90 days. Since a delay in treatment may allow for additional tumor progression, we determined the time from abnormal radiograph to diagnosis and therapy for patients diagnosed with SCLC in a tertiary referral center.

Methods Used: Forty five consecutive patients diagnosed with SCLC between 2004 and 2008 with adequate documentation of evaluation, diagnosis and treatment were included in this analysis. Results are reported as mean (median) $\pm$ SD.

Summary of Results: The study population had a median age of 67 (69) $\pm$ 11 yrs (range 45–88). 51 percent were women, 73% Caucasian, 27% African American and 100% were current or former smokers. Eighteen of 45 patients (40%) presented to the emergency department for evaluation. Disease stage was extensive in 27/45 patients (60%). Time from first abnormal radiograph to tissue diagnosis was 20 (11) $\pm$ 24 days (range 1–93). Time from first abnormal radiograph to initiation of treatment was 35 (35) $\pm$ 26 days (range 1–103). Thirty six patient have died, with the time from initial abnormal radiograph to death of 294 (260) $\pm$ 245 days (range 14–986). Nine patients are currently alive, and seven of these have had relapse of their disease. Eight patients (18%) had a chest radiograph interpreted as normal within 6 months preceding the diagnosis of SCLC.

Conclusions: The time interval from abnormal radiograph to initiation of treatment for SCLC in this single center study overlaps with the reported doubling time for SCLC. The likelihood of cure of SCLC was low, consistent with previous reports.

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IDENTIFYING THE ROLE OF ESTROGEN IN ONCOGENESIS

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Purpose of Study: Breast, thyroid and lung cancers are among the group of tumors which demonstrate strong female preponderance. However the molecular mechanisms for this observation are unclear. We hypothesize that circulating estrogens activate and maintain cellular proliferative pathways during oncogenesis.

Methods Used: The neoplastic cell lines, NPA'87 and DRO'90 were exposed to vehicle or estradiol (2.2x10⁻⁹ M) for 48 hours, after which cellular proliferation was determined by BrdU and MTT assays. Specificity of estradiol (E2) activity was determined by using the estrogen receptor-alpha antagonist, ICI 182780. Erk1/2 activity was determined using a kinase assay. MEK activation was determined by measuring levels of phosphorylated MEK. All experiments were repeated after BRAF knockdown using siRNA. Proliferation experiments were repeated in the presence of the small molecule BRAF inhibitor BAY-43-9006 in DRO cells.

Summary of Results: Compared to vehicle, E2 increased proliferation of DRO by 21.6% (p < 0.01) and NPA by 21.8% (p < 0.01) in 24 hours. ICI 182780 significantly attenuated E2-induced DRO cell proliferation (8.2%), but had no effect on NPA proliferation (18.6%). E2 increased levels of phosphorylated MEK in DRO cells after 3 hours and in NPA cells after 1 hour. The ERalpha antagonist attenuated MEK phosphorylation in NPA cells and to a lesser extent in DRO cells. E2 increased Erk1/2 activity in both cell lines. ICI had no effect on Erk1/2 activity in DRO cells, but attenuated Erk activity in NPA cells. BRAF knockdown by siRNA attenuated E2-induced Erk1/2 (24 hours) activity in DRO cells, and abolished E2-promoted proliferation in NPA cells. Inhibition of BRAF by BAY-43-9006 abolished E2-promoted proliferation in DRO cells.

Conclusions: Estrogen significantly increased proliferation in both cancer cell lines. Proliferation was partially dependent on ER alpha in DRO but not NPA cells. In addition, estrogen appeared to increase Erk and MEK activity in both cell lines. BRAF knockdown attenuated E2 - induced ERK1/2 activation and proliferation in DRO cells. We conclude that estrogens may regulate proliferation of cancer cells through BRAF dependent signaling.

Therefore E2-dependent pathways may be potential targets for adjuvant cancer therapy.

Infectious Diseases I

Concurrent Session

2:00 PM

Friday, February 26, 2010

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A RETROSPECTIVE REVIEW OF AUTOPSY BLOOD CULTURES AT LSUHSC NEW ORLEANS

A. Collinsworth, R. McGoey *Louisiana State University School of Medicine, New Orleans, LA.*

Purpose of Study: The utility and significance of blood cultures drawn at autopsy have long been debated. There currently exists no standard for differentiating pathogens from contaminants or for determining the clinical significance of certain pathogens. The aim of this study is to review blood culture results from autopsies performed over an 18 month period and to evaluate each case for clinical correlation and antemortem concordance or discrepancy.

Methods Used: Sixty-nine individuals who underwent autopsy examination by the LSU Department of Pathology from 1/1/08–9/1/09 were identified and selected based on availability of both antemortem and postmortem blood culture results.

Summary of Results: 29% (20 of 69) of cases had no growth from postmortem blood culture. Of these, 70% (14) had negative blood cultures prior to death. 71% of autopsy cases (n=49) had postmortem blood culture positivity. The most commonly detected microorganisms included *Candida* spp. (17 of 49), *Enterococcus* spp. (15 of 49), coagulase-negative *Staph* spp. (11 of 49) and *S. aureus* (6 of 49). In 71% of autopsy culture-positive cases, a single organism was isolated. In 22 cases (45%) there was congruence between ante- and postmortem microorganism identification. In all 17 cases of post-mortem detection of *Candida* spp., there was no evidence for antemortem blood culture positivity for yeast; however, 3 cases had documented histopathological evidence of invasive *Candida* spp. and in 2 cases there was antemortem culture sputum and urine culture positivity for *Candida*. In only 2 cases of postmortem *Enterococcus* bacteremia was there antemortem confirmation of *Enterococcus* bacteremia. In all six cases where post-mortem *S. aureus* was detected, there was documented *S. aureus* bacteremia prior to death.

Conclusions: The examination of postmortem blood cultures is useful when combined with clinical correlation and histopathological data. Negative autopsy blood cultures are predictive of antemortem negative cultures. Autopsy blood cultures that reveal *S. aureus* are specific for antemortem bacteremia. The absence of any cases of *Candidemia* detected prior to death may suggest missed diagnoses in light of the histopathological findings in autopsy tissues. The significance of post-mortem coagulase-negative *Staphylococcus* may be under appreciated.

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RARE BUT THERE: CONGENITAL SPHINGOMONAS PAUCIMOBILIS SEPTICEMIA

MC. Mbamalu, D. Macariola *East Tennessee State University, Johnson City, TN.*

Case Report: A 2100 gram, 34-week, preterm white male delivered to a 19-year-old gravida 1 mother. The pregnancy was complicated by premature contractions at 30-weeks' gestation, maternal tobacco use, urinary tract infection and chorioamnionitis. Mom was admitted in preterm labor with a white blood cell count of 32,000: 83% neutrophils, 15% lymphocytes. Maternal Group B streptococcus culture was positive and she received ampicillin and gentamicin prior to delivery. Other prenatal laboratory reports were unremarkable. Histopathology study of the placenta confirmed chorioamnionitis. Empiric antibiotics with ampicillin and amikacin were started immediately post delivery in the Neonatal Intensive Care Unit (NICU) after blood cultures. On initial physical exam, the baby had mild tachypnea and retractions. The rest of the physical examination was unremarkable. Blood cultures grew *Sphingomonas paucimobilis*, susceptible to amikacin. Cerebrospinal fluid studies were negative. The baby completed 14 days of amikacin and ampicillin and was discharged home in satisfactory condition.

Discussion: *Sphingomonas paucimobilis* is a member of the relatively newly defined gram-negative, strictly aerobic, chemoheterotrophic bacteria called sphingomonads. *S. paucimobilis* has played a role in human disease, primarily nosocomial non-life-threatening infections. Lemaître et al. reported isolation of *S. paucimobilis* from tracheal secretions of mechanically ventilated babies in the NICU which was attributed to the ventilator temperature probes. None of the neonates developed pneumonia or sepsis. Our case illustrates congenital sepsis in a patient that was never intubated and whose only invasive procedure was placement of an umbilical vein catheter under aseptic conditions. This case serves as a reminder to pediatricians and neonatologists that *S. paucimobilis* can present as a congenital infection and the burden of disease caused by this organism may not be limited to asymptomatic nosocomial infections but can be congenital and symptomatic.

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THE CHANGING EPIDEMIOLOGY OF INVASIVE H. INFLUENZAE DISEASE IN METROPOLITAN ATLANTA IN THE HIB VACCINE ERA, 1989–2007

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Purpose of Study: An effective *Haemophilus influenzae* type b (Hib) conjugate vaccine was licensed in 1987 for use in children in the U.S. and expanded to universal infant use late in 1990. We seek to describe long term changes in the epidemiology of invasive *H. influenzae* (HI) disease after Hib vaccine introduction.

Methods Used: Population-based, active surveillance was conducted for invasive HI in metropolitan Atlanta, GA between 1/1/1989 and 12/31/2007. A case was defined as isolation of HI from a normally sterile site. Medical records were reviewed. Serotyping of isolates was performed by slide agglutination and confirmed by capsule-gene PCR. US Census data were used for calculating incidence rates.

Summary of Results: A total of 1145 cases of invasive HI were identified during '89–'07. Between '89 and '07, there was a significant reduction in the overall rate of invasive HI disease (5.0/100K in '89–'90, 1.2/100K in '06–'07, $p=0.0002$ χ^2 trend) and Hib disease (2.5/100K in '89–'90, 0.01/100K in '06–'07, χ^2 trend $p=0.009$). The rate of HI among children <5 years decreased from 44.8/100K in '89–'90 to 2.8/100K in '06–'07 (χ^2 trend $p<0.0001$). No significant change in the rate of HI among adults ≥ 18 years was observed (1.9/100K in '90, 1.4/100K in '06–'07).

The mean age of cases increased from 13.8 years in '89 to 45.4 years in '07. In '89, 61% of disease occurred in children <2yrs of age; in '07, 65% of disease occurred in adults >40 yrs of age. Among isolates serotyped in '89, 84% were serotype b, 14% nontypeable (NT) and 1.4% serotype f (no types a, c, d, or e) vs. 60% NT, 30% type f, 7.5% type e and 2.5% type a (no type b) in '07. Between '00–'07, 35% of cases had bacteremia without focus, 49% bacteremic pneumonia, and 7% meningitis; 72.6% had one or more underlying medical conditions. The overall in-hospital mortality rate was 12% and was highest in the elderly (> 65 yrs, 21%) and those with bacteremia without focus (20%).

Conclusions: Since introduction of the Hib vaccine, the incidence of invasive HI and Hib disease has decreased significantly. Invasive HI is now predominantly a disease of older adults with bacteremia with or without pneumonia due to nontypable and non-b encapsulated strains.

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HOSPITALIZED CHILDREN WITH NOVEL H1N1 INFLUENZA A INFECTION IN MEMPHIS, TN 2009

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Purpose of Study: Following the beginning of school in the summer of 2009 in Memphis, Le Bonheur Children's Medical Center (LBCMC) experienced a sharp rise in the number of children admitted with infection caused by novel H1N1 influenza A virus. Our aim is to describe this early period of LBCMC's influenza pandemic experience and identify patterns useful for improving clinical care of patients with novel H1N1 infections.

Methods Used: Patients admitted between 9/1/09 and 10/5/09 with confirmed influenza A infection were eligible for enrollment. A complete roster of subjects was established using: 1. Admission lists from house staff

and PICU 2. All influenza testing by rapid antigen 3. Positive influenza testing by PCR. After case identification, clinical data for each subject was collected and analyzed using SAS software.

Summary of Results: A total of 147 subjects were identified and data for 144 were analyzed. Sensitivity of influenza testing by rapid antigen was 50%. A random sample of PCR positive specimens was confirmed by PCR as novel H1N1 using H1N1 specific primers. Primary reasons given for presentation to emergency department included fever (42%) and respiratory distress (25%). 99 (69%) subjects had underlying conditions: 46 (32%) with asthma and 14 (10%) with prematurity. Patients with and without underlying conditions had approximately the same rate of ICU admission (14 vs 13%). Of the 20 (14%) patients admitted to ICU, 1 required oscillatory ventilation and ECMO, and 3 died. The median duration of hospital stay was 2 days with no difference found between those with and without underlying conditions. Complications included 43 (30%) patients with pneumonia. 94 (65%) patients received at least one dose of antibiotics.

Conclusions: Our data indicate that most admissions for ILI are short. When complications are present, however, they can be severe and require ICU management. The majority of patients admitted have underlying conditions, but the presence of an underlying condition is not a reliable predictor of ICU admission. Children with asthma are of particular concern as they are highly represented in our sample. Pneumonia is a common complication and more investigation is required to determine the etiology of influenza-associated pneumonia in this population.

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EPIDEMIOLOGY OF INVASIVE PNEUMOCOCCAL DISEASE IN ATLANTA, 1998–2007

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Purpose of Study: Pneumococcal disease is a leading cause of respiratory disease and meningitis in children and adults throughout the world. A 7-valent pneumococcal conjugate vaccine (PCV7) was introduced for universal use in infants in the U.S. in 2000. We describe the epidemiology of invasive pneumococcal disease (IPD) in Atlanta in the years following PCV7 introduction.

Methods Used: Population-based, active surveillance for IPD was conducted in the Atlanta metropolitan statistical area (MSA). Cases were defined as isolation of *S. pneumoniae* from a normally sterile body site in a resident of the Atlanta MSA. Isolates were serotyped by the Quellung reaction. PCR testing was done on some serotypes to differentiate them within a serogroup. Incidence rates were calculated per 100,000 population using US Census data population estimates. X2 trend was used to determine significant ($p < 0.05$) changes in incidence rates.

Summary of Results: A total of 7,473 cases of IPD were identified from 1998–2007. Among children, the median age was 16 months, 57.56% were male, 40.87% were white, 44.39% were black and the case fatality rate was 1.55%. Among adults, the median age was 54 yrs, 53.14% were male, 52.10% were white, 43.51% were black, and the case fatality rate was 14.55%. The most common clinical syndrome in children was bacteremia without focus (55.57%) and in adults, bacteremic pneumonia (69.46%). There was a significant decline in the incidence of IPD due to the PCV7 serotypes (14.8/100K in 1998, 0.8/100K in 2007 [$p < 0.0001$]). Incidence of IPD caused by six additional serotypes (to be included in the new PCV-13 vaccine) increased from 3.7 in 1998 to 4.4 in 2007 ($p < 0.0001$) (representing 15.8% of IPD in '98 and 40.2% of IPD in '07). Incidence of all other serotypes increased from 4.8 in 1998 to 5.7 in 2007 ($p < 0.0001$).

Conclusions: Rates of IPD due to PCV7 serotypes have declined significantly for patients of all ages, race and gender. Modest increases in the rates of IPD due to non-PCV7 serotypes have been noted. The anticipated introduction of PCV-13 should cover at least 40% of remaining IPD in Atlanta. Continued surveillance will be necessary to monitor serotype trends over time.

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QUALITATIVE AND QUANTITATIVE EVALUATION OF A PCR-BASED DIAGNOSIS OF PERTUSSIS IN CHILDREN

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Purpose of Study: Pertussis is an under-recognized serious infection of children and adults. Proper diagnosis and treatment ablates epidemics. Conventional diagnostics are insensitive and are impaired by antibiotics. Severity varies widely and is not predictable. RealTime PCR may allow improved detection and quantification of bacterial load. We therefore developed a pertussis PCR test and evaluated it vs. conventional culture, and the relationships between disease severity and bacterial load.

Methods Used: Records of all pertussis+ tests submitted from LeBonheur (2/2/04–5/26/09) were collected (N=104). For every 3rd consecutive (+) test, the nearest (–) test was also collected (N=35). For quantitative validation, PCR cycle threshold (Ct) was compared to quantitative culture.

Summary of Results: 43 samples were tested both by PCR and culture. The PCR was (+) in 14/14 in which the culture was (+). Culture was falsely (–) in 20 samples. Compared to PCR, the sensitivity of the culture assay was 41% (specificity=100%). Compared to PCR–, patients whose samples were PCR+ had longer hospitalizations (mean 4.27 vs. 2.15 days, $P = 0.0285$), greater likelihood of paroxysmal cough ($P = 0.0167$) and cyanosis ($P = 0.0002$), greater mean % lymphocytes (66% vs. 40%, $P < 0.0001$), and greater absolute mean lymphocyte counts (14 vs. 6, $P = 0.0016$). Those who's vaccines were “up to date” through 4-months were less likely to have PCR+ pertussis vs. those who were not ($P = 0.0013$). PCR reliably quantified bacterial load. Ct values from cultured *Bordetella pertussis* correlated with colony count ($P < 0.0001$, $r^2 = 0.913$). Ct values of the same clinical sample (N = 70) repeated on different PCR runs were nearly identical ($P < 0.0001$, $r^2 = 0.989$). Higher bacterial load correlated with clinical outcomes of longer duration of hospitalization ($P = 0.0003$), lymphocyte count ($P = 0.0061$). Likely reflecting vaccination status, increasing age correlated with decreasing bacterial load ($P = 0.0013$).

Conclusions: Our PCR assay reliably detects children with clinical pertussis and is significantly more sensitive than the conventional diagnostic technique (culture). PCR quantification of bacterial load was reliable, reproducible and predicted clinical disease severity.

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MOLECULAR DIAGNOSIS OF MYCOPLASMA PNEUMONIAE FOR PEDIATRIC SPINAL FLUID

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Purpose of Study: *Mycoplasma pneumoniae* is considered the most commonly diagnosed pathogen in encephalitis but serological tests do not provide rapid diagnosis. Molecular probes have been used with mixed experiences to date. Our purpose was to determine the specificity of a *M. pneumoniae* molecular probe in CSF and prevalence of positivity in undifferentiated pediatric encephalitis syndromes.

Methods Used: Group A. Convenience samples of CSF from pediatric patients in 2006 to 2008 with confirmed bacterial meningitis were used to determine probable specificity of the molecular probe. Group B. To determine prevalence of probe positivity in pediatric encephalitis patients, CSF samples from 2008 which had negative PCR results for enteroviral and HSV were evaluated by molecular probes for *M. pneumoniae*. Real time PCR with Taqman technology was used. Electronic medical record reviews were done for all samples. All patients were from Arkansas Children's Hospital.

Summary of Results: Group A. Isolates from 13 patients with proven bacterial meningitis were examined. They had a mean age of 5 years (range 2 months to 17 years). All of these specimens were negative for *M. pneumoniae* by molecular diagnosis. (specificity of 100%). There were an additional 13 patients (Group B) with undifferentiated encephalitis with no diagnosis by serology, molecular probe or culture of another pathogen. They had a mean age of 5.7 years (range 1 year to 10.75 years). No positive isolates were found in this group. Of the 13, only 3 patients had serology with 1 patient having positive IgG and a low positive IgM. No other patients had a positive IgG or IgM. 2 patients had a negative mycoplasma serology. It is suspected that the prevalence of *M. pneumoniae* is low but the sensitivity is unclear due to very small number of suspected cases in this series and the infrequency of definitive serology performed in this retrospective collection. Timing of specimen collection and use of antibiotics are other considerations to explain negative results.

Conclusions: Preliminary conclusions suggest that PCR for *M. pneumoniae* did not identify this agent as a common cause of pediatric encephalitis. Sensitivity of this assay needs to be determined in a larger number of proven cases of *Mycoplasma pneumoniae* encephalitis.

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LINEZOLID USE AT A CHILDREN'S HOSPITAL

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Purpose of Study: The purpose of this study was to review appropriate use of Linezolid at the tertiary care children's hospital.

Methods Used: Records of 15 children who were admitted between 11/8/08 and 2/24/09 and prescribed Linezolid were reviewed as part of a pharmacy audit for quality improvement.

Summary of Results: In 5 children ORSA was isolated, in one OSSA (plus 3 other organisms), in 2 S.pneumoniae, in one 5 different gram negative enteric were isolated and in 6 no organism was isolated. There were 5 SSTIs all caused by S. aureus, including one in which multiple organisms were isolated, one ear drainage grew ORSA, one HUS with pleural effusion grew S. pneumoniae from blood and there were 7 pneumonias (6 with pleural effusions) and in only one case S. pneumoniae was identified from a pleural effusion.

Eleven children were admitted to the hospitalist service, 2 to community pediatrician service, one each to Hematology/Oncology and Infectious Diseases (ID) services. Of the fourteen children not on ID service, ID was consulted in 11 children. Of the 12 children with ID involvement Linezolid was recommended in nine with reason documented in only three and stopped in two. Reason for Linezolid use was documented in one of the three patients with no ID involvement. In 9 patients with ORSA, OSSA or S. pneumoniae isolates all were susceptible to Vancomycin and in 5 to Clindamycin. All S. aureus isolates were susceptible to TMP/SMX and both S. pneumoniae isolates were susceptible to Cefotaxime and Ceftriaxone.

The reasoning for starting or continuing Linezolid was appropriate in one of three without ID involvement and in 8 of 12 children with ID involvement the reason for Linezolid use did not appear appropriate. The ID service continued with Linezolid started by the consulting physician and because the patient was being treated with Linezolid and were showing clinical improvement.

Conclusions: Linezolid was started empirically without good reason. ID specialists were not willing to recommend change. To improve appropriate Linezolid use it appears that the best intervention is at the time of starting Linezolid. Pharmacist with the support of ID specialist should if appropriate recommend alternative to Linezolid at the time it is ordered.

Medical Education and Medical Ethics

Concurrent Session

2:00 PM

Friday, February 26, 2010

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COMMUNITY TRAINING IN PEDIATRIC ALLERGY CLINICS USING HIGH FIDELITY SIMULATION DEMONSTRATES IMPROVED PREPARATION FOR OFFICE EMERGENCIES

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Purpose of Study: To determine if case-based simulations with high fidelity mannequins are effective in teaching and retention of emergency management team skills.

Methods Used: Two allergy clinics in Little Rock were invited to ACH PULSE (Pediatric Understanding and Learning through Simulation Education) center for a one day workshop to evaluate their skills in regard to the management of pediatric allergic emergencies and practice emergency team training skills. A Clinical Emergency Preparedness Team Performance Evaluation (CEPTE) was developed in order to evaluate the competence of the teams in several areas: leadership/role clarity, closed loop communication, team support, global assessment and scenario specific skills. Four cases were developed around common pediatric allergic emergencies, and the clinic staff participated in each case using medical simulation with high fidelity mannequins. They were evaluated as to whether a skill was not done, attempted, or complete by multiple reviewers using video recording. Nine to twelve months post initial training, a

single ambush case using a mobile mannequin was performed in the clinic to determine retention of the skills training.

Summary of Results: Results were acquired from 3 separate evaluators and analyzed using a student's t test. P values were significant for both clinics ($p < 0.005$) for role clarity, communication, scenario specific skills, and totals for the scenario between all the cases when compared to the first case. Both clinics showed marked improvement throughout the day when all areas of interest were included ($p < 0.05$). Follow up scenarios demonstrated retention of skills training at both clinics. ($p = 0.004$ for both).

Conclusions: CEPTE scores demonstrated improved team management skills with simulation training in office emergencies. Significant recall of team emergency management skills was demonstrated months after the initial training. This may suggest that hands on high fidelity mannequins are an effective method for teaching clinicians emergency management team skills and preparation for office emergencies.

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AN INTERACTIVE WEB-BASED PROJECT TO STIMULATE INTERNAL MEDICINE RESIDENT READING USING BOARD TYPE QUESTIONS

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Purpose of Study: Restricted resident hours prompted us to seek alternative methods to supplement traditional teaching. Electronic learning (e-learning) has definite practical advantages, especially during professional education with long work hours and a variable work schedule. However, the best use of e-learning remains unclear.

Methods Used: One Internal Medicine faculty member sent four clinical case-based questions per week through the e-mail to all internal medicine residents. The residents returned the answers by e-mail before midnight that day. On the next day the faculty member discussed each question and replied to individual residents to stimulate discussion. All questions and responses were saved in an electronic folder and analyzed weekly to track the percent participation, the percent correct, frequency of electronic interaction between the residents and the faculty sponsor, and the content areas with low scores. We used an anonymous survey to learn the residents' opinion about this program.

Summary of Results: These results cover the first six months of this project with 46 question sets. The mean percent participation on a set of questions was 67% with a range of 43% to 97%. The mean percent correct on all questions for all residents was 71.3 % with a range of 15% to 100 % different questions. There was no significant difference in the percent correct in the three resident training levels. Sixty seven percent of the question sets resulted in an electronic interaction between the residents and the faculty sponsor. Ninety-six percent of the residents found the program useful. Seventy-eight percent said they routinely looked up answers before submitting their answer. Eighty-seven percent thought that the answers provided by the faculty sponsor stimulated reading. The faculty sponsor spent 45 to 120 minutes per week on this activity.

Conclusions: Most Internal Medicine residents in our program participated in this web-based project. This program increased overall reading since it did not replace any traditional activity. It provided practice with clinical board-type questions and stimulated interaction with the faculty sponsor. Follow-up departmental conferences will review content areas with low percent correct answers. The time demands on the faculty sponsor are relatively high.

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IMPROVING PEDIATRIC MORNING REPORT

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Purpose of Study: Serving educational needs of diverse learners, Pediatric Morning Report (PMR) is a daily teaching session focusing on patient care. We used ecologic momentary assessment (a brief, unobtrusive method of evaluation immediately following an educational experience) to collect feedback from participants to evaluate the quality of PMR and identify opportunities to improve. Our goals were to define the highly-rated components of PMR to identify what learners valued and what areas might be improved, while comparing faculty and housestaff experiences.

Methods Used: Evaluation cards were distributed to PMR participants from December 2008 through August 2009 following each session. Cards for faculty/fellows (FAC) and housestaff (HS) included: residents' time was well spent in morning report, there were clear teaching points, resident/faculty engagement was excellent. Responses: strongly agree (SA)/ agree (A) / disagree (D) / strongly disagree (SD). Questions also asked what would improve the presentation (PowerPoint, more cases, subspecialist presence, journal article, other). We used chi-square analysis to compare groups' responses.

Summary of Results: PMR sessions totaled 176, with average attendance of 9.3 FAC and 17.9 HS. HS completed 461 cards (over 122 days): 44% post-graduate year 1 (PGY1), 29% PGY2, 27% PGY3/4. FAC completed 197 cards (90 days): 87% peds faculty, 8% non-peds faculty, 5% peds fellows. FAC and HS differed significantly on all items rated (table) at $p < .001$. Among HS, ratings were highest from PGY2s and lowest for PGY3/4 (time was well spent: SA for PGY1 76%, PGY2 82%, PGY3/4 67%). Approximately 1/3 of respondents (both groups) indicated desire for subspecialty presence; approximately 1/5 desired discussion of more cases. History and physical components were rated least valuable; differential diagnosis and management were most valued by both groups.

Conclusions: Ratings of PMR were significantly different among participants. Components valued by FAC and HS were similar, as were ways suggested to improve PMR.

	Housestaff		Faculty	
	%SA	%A	%SA	%A
Time Well Spent	75.1	23.2	52.1	36.6
Teaching Points	72.4	24.8	46.7	40
Residents Engaged	59.7	30.5	22.2	51
Faculty Engaged	63	30.5	34.3	35

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BARRIERS TO ACCULTURATION OF INTERNATIONAL MEDICAL GRADUATES IN PEDIATRIC RESIDENCY TRAINING

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Purpose of Study: The degree of acculturation of international medical graduates (IMGs) is manifested in the way they perceive the concepts, beliefs and values that are taken for granted by US graduates (USGs). IMGs experience challenges at work including communication with patients, interactions with staff and technology and then go home to a displaced environment where their transitional challenges continue. IMGs might benefit from program changes that enhance transition into the US culture and academic milieu. The purpose of this qualitative study was to identify perceived barriers to this transition.

Methods Used: PL-1 and PL-3 IMGs participated in separate focus groups at the end of the 2008-2009 academic year. The two groups were selected to reflect incoming residents' challenges and outgoing residents' adaptations. Data were analyzed by two sociology faculty with expertise in qualitative study.

Summary of Results: Both groups reported work-related and non-work challenges upon arrival to the US. Work challenges involve issues with medical insurances, learning about documentation, medico-legal liability, and communication. Language fluency and accents lead to misinterpretation, particularly with nursing staff and patients. Varied gender roles, shy demeanor and 'speaking when spoken to' are cultural practices that are often misinterpreted by peers and faculty. Non-work challenges include difficulty in obtaining social security numbers, apartments, driver's license and insurance. IMGs felt their initial year of training was more about acquiring skills to live in America than about acquiring academic knowledge. A suggested intervention was that IMGs be on a lighter clinical rotation initially and have temporary housing. Graduating residents perceived peer confidence in their abilities and hard work over time helped overcome the communication problems rather than any learned changes in accent or language.

Conclusions: Understanding the barriers faced by incoming IMGs can help guide strategies to promote efficient acculturation allowing IMGs to focus on their pediatric education earlier.

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NURSE ATTITUDES REGARDING INTERNATIONAL MEDICAL GRADUATES

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Purpose of Study: Work challenges for international medical graduates (IMGs) may include communication with patients, interaction with nursing and allied health care staff and technology used for documentation. A prior qualitative study with IMGs revealed communication with nurses as a significant barrier to the transition of residents into the American work culture and the IMG-nurse work relationship as a source of distress for members of the health care team.

Methods Used: Nurses reported their perception of the strengths and weakness of IMGs as compared to US graduates (USGs). Information was collected via survey. A total of 80 surveys was distributed and 44 responses were obtained (55%).

Summary of Results: Twenty out of 46 nurses (43%) on the general pediatric floor, 16 of 22 (73%) emergency room and 8 of 12 (67%) outpatient nurses replied. All 44 nurses had worked with IMGs, and reported they would work with an IMG if given a choice. Sixty-one percent of nurses agreed that they enjoy working with IMGs while 39% were neutral. Some of the strengths noted about IMGs include: 1) being multilingual they are an asset in communicating with patients from other countries and cultures; 2) they are more likely to be culturally sensitive and show patience with families that have language problems; 3) likely to be more knowledgeable, efficient and less arrogant as compared to USGs. A unanimous weakness identified was language difficulties and hence communication barriers between staff or patient families and the resident. Asked if they bypassed an IMG resident when seeking help with their patient, both inpatient and outpatient nurses reported that in the interest of time efficiency they were likely to bypass an intern (IMG and USG) and ask the senior resident as the intern lacks sufficient experience and would have to ask the senior for advice ultimately. Communication was a less frequent reason to bypass the intern. When rating USGs and IMGs for various attributes, the nurses felt IMG residents were eager to learn, patient, sincere, reliable and culturally more sensitive as compared to a USGs. An IMG was more likely to have communication problems, and weaker interpersonal skill and bedside manner as compared to the USG resident.

Conclusions: Next steps include incorporating information about nursing attitudes regarding IMGs to focus on communication skills into a pediatric medical acculturation curriculum.

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PEDIATRIC PALLIATIVE CARE INSTRUCTION FOR RESIDENTS: AN INTRODUCTION TO IPPC

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Purpose of Study: This study used the Initiative for Pediatric Palliative Care (IPPC) curriculum to train key interdisciplinary staff and faculty and ascertain the perceived benefits of this model.

Methods Used: A one day retreat using the IPPC curriculum was held to provide training in relational communication, cultural humility, pain and symptom management, family-centered care, interdisciplinary team problem solving and planning for subsequent resident education at unit level in the ED, NICU, PICU and Cardiology Services. Two bereaved parents were co-learners and trainers. Educational methods included traditional lecture, video-tape instruction, small group case-based and interdisciplinary discussions, a facilitated Parent-Panel, and a unit-based strategic planning session for future hospital-based and resident/fellow education. Pre- and post-training measures were solicited from all participants reflecting on methods, content and self-reported palliative care confidence.

Summary of Results: 26 interdisciplinary staff (7 MD, 8 RN/APRN, 4 SW, 3 CCLS, 2 chaplains & 2 bereaved parents) participated. The evaluations (5-point Likert scale) noted: Mean scores >4.0 in new knowledge gained, value in collaborative learning with health care professionals and families, as well as with professionals from different disciplines, value in small-group learning, session leadership and ability to work with professionals outside participants' own unit. Areas with mean scores >3.5 but <4.0 included the sessions' ability to enhance individuals' PPC knowledge, skills & attitudes, or increase confidence to facilitate sessions on their own. However, the session did increase individuals' confidence to advocate for improved PPC (4.6 $\pm$.4) and in particular the plenary entitled "A Relational Approach to

Communication,” the presence of family members in small groups, and the use of case-based, as well as video-tape triggered learning and discussion were all considered valuable.

Conclusions: Providing PPC education can be accommodated in a well planned 1-day interdisciplinary continuing education experience. The IPPC curriculum provides excellent content and formats for this. Incorporation of family-members as co-learners and teachers in such a setting is valuable. PPC advocacy within the hospital can be an expected outgrowth of this type of educational experience.

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PEDIATRIC PALLIATIVE CARE: FEEDBACK FROM PEDIATRIC INTENSIVISTS

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Purpose of Study: To inquire of pediatric intensivists what they thought the role of pediatric palliative care (PPC) was in the Pediatric Critical Care Unit (PCCU).

Methods Used: A 25 question survey addressing demographics, clinical experiences, educational experiences, barriers/resources, and opinions of palliative care services was distributed to 719 members of the AAP Section on Critical Care by email.

Summary of Results: 102 members (14%) completed the survey. Their gender was 51% male, average age 46 years, and in practice for 20 years; most of their professional time was spent in clinical practice. Respondents felt comfortable treating patients who were dying; most “very confident” responses came with typical PCCU interventions (informing a family of prognosis, communication, discussing a shift in treatment goals, and treating common symptoms in a dying patient). Those actions that reached outside of the PCCU (placing a patient into hospice, making use of services to support the dying child and family), received lower average confidence ratings. Over ½ of respondents reported feeling “very confident” managing symptoms of the dying child, and no respondents rated themselves as less than “confident” (confidence in treatment was higher if the symptom was more acute in nature, e.g. seizure, pain). The perceived usefulness of various educational interventions to teach palliative care skills were surveyed. Traditional didactic methods were assigned the lowest scores; informal methods (e.g. trial and error, self-guided learning, and learning from a role model) ranked the highest. The educational methods experienced most frequently ranked as more useful.

Conclusions: The potential uses of PPC services in the PCCU were ranked: most helpful were services that dealt with continuity between hospitalizations, transition to a community setting, and provision of bereavement care or counseling for family and staff. Of note, a service that is typically associated with palliative care consultation, assisting in the withdrawal of life-continuing treatments, was ranked the least helpful. Potential objections to the provision of PPC included respondents not wanting to “consult out the care of the dying patient” and feeling confident in their own skill set to not require any PPC consultation.

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ADDRESSING AND PREVENTING STRESS, FATIGUE AND BURNOUT IN HEALTH CARE PROVIDERS

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Purpose of Study: Maintaining humanism is challenging for health care providers (HCP), especially when experiencing stress. ACGME recognizes negative effects of stress and recommends policies to prevent and counteract it. We instituted weekly Relaxing, Rejuvenating, Rejoicing in Residency sessions (RRRinRS) with the following objectives: (1) assess and monitor stress/fatigue/burnout among residents over 3years, evaluate the effectiveness of RRRinRS intervention (2) Evaluate effectiveness of RRRinRS as means for recovery and fatigue/burnout prevention (3) Develop process for identifying residents at highest risk of burnout (4) Needs assessment for development of stress/recovery management training.

Methods Used: RRRinRS are held in-hospital and are open to all HCP. Sessions provide encouraging environment to share information through personal stories, book reviews, poetry, etc. Secure internet surveys were administered to medicine residents and core faculty and repeated quarterly to track responses. Surveys gathered qualitative data (general perceptions of

personal stress/coping strategies) and quantitative data (stress, physical fatigue, burnout, life satisfaction, general health, coping styles, negative affectivity).

Summary of Results: Respondents (response rate = 45%) indicating higher number of attendances reported significantly lower levels of exhaustion and pressure related stress ($r = -.53/- .59$, respectively, both $p < .01$). Respondents with higher levels of negative affectivity reported higher frequencies of nonoptimal forms of coping (Avoidance and Emotional coping, $r = .48/.49$, respectively, $p < .01$) and indications of resource drain and strain. High negative affectivity was associated with higher levels of perceived stress. Qualitative evidence supported these coping behaviors, illustrating a need to teach residents more active problem focused coping techniques.

Conclusions: Preliminary results suggest that those who more frequently attended RRRinRS reported lower levels of stress than those who attended fewer sessions. Qualitative data provide insights into how HCP are recognizing and responding to stress. This data provides support for continued efforts to further refine and comprehensively evaluate the intervention as a strategy for improving stress and recovery management.

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MEDICAL HUMANITIES: STUDENT CHOICES AND REFLECTIONS

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Purpose of Study: The purpose of this study is to provide a descriptive analysis of the medical humanities activities selected by first-year medical students.

Methods Used: The study employed a mixed methods approach. Course directors provided students with possible medical humanities activities. Students were also encouraged to develop their own activities relevant to the medical humanities. All students participated in these activities as a component of a required course in the first-year curriculum. Upon completion of these activities, students provided a critical reflection of their experiences in the form of written portfolio entries. The researchers collected and analyzed the data reported in the current study. The data are part of a larger portfolio-based assessment required by all first-year students. Medical humanities activities were cataloged according to medium of presentation. The researchers calculated frequencies and percentages of all reported medical humanities activities. A rubric was developed to guide selection of written portfolio pieces. Excerpts from selected portfolios are included in the study to provide a narrative description of student experiences.

Summary of Results: Data was collected over a period of two years. The total sample size included 150 first-year medical students. Preliminary data indicated that 72 first-year students completed a total of 260 humanities activities. Popular humanities categories included films (21.15%), articles/essays/short stories (16.92%), and exhibits (15.00%).

Conclusions: Medical students selected diverse medical humanities activities. This study provides useful information for the development of medical humanities curricula. Using a portfolio-based assessment system encourages collaboration between faculty and students by providing open channels for reciprocal feedback. This research may help to ensure a richer educational experience for medical students.

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DOULAS AND RESIDENTS TOGETHER (DART) PROGRAM: NOVEL EDUCATIONAL APPROACH TO TEACH BREASTFEEDING AND CULTURAL COMPETENCY TO RESIDENTS

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Purpose of Study: Doulas are experienced professionals who emotionally support mothers prenatally, natally and post-partum. Doulas consider breastfeeding education important to their work. Pediatric residents usually receive this education in the newborn nursery and outpatient clinics, but not in the patient's home. This project evaluated the impact on residents' knowledge of breastfeeding and cultural competency after exposure to community outreach doulas during prenatal breastfeeding classes and home visits.

Methods Used: During a one month community-based advocacy rotation between August 2007 and August 2009, residents were enrolled in the DART Program. Residents reviewed a doula website to learn about their profession, and completed an on-line cultural competency module from the Office of Minority Health. They then attended a prenatal class with doulas from United Cerebral Palsy and mothers in an obstetric clinic for low income, predominantly minority women. Subsequently, residents scheduled a postpartum home visit with a doula. At the rotation's conclusion, residents completed a written questionnaire about their experiences. Residents' comments were analyzed for common themes.

Summary of Results: Twenty one of 22 enrolled residents noted improved knowledge of breastfeeding, including enhanced ability to teach it. All residents learned about community resources and economic and familial obstacles facing these families. Four of six who attended home visits wanted to act more as observer than teacher. Another was not allowed inside the patients' home, but talked to her outside. One "loved the home visit." Sixteen were unable to attend a home visit due to scheduling conflicts or misunderstood rotation directions. Two desired more opportunities to visit clients' homes, and several wanted more time to reschedule missed home visits.

Conclusions: Linking pediatric residents with community based doulas is a novel educational approach to teach breastfeeding and enhance cultural competency taught on-line. The majority of the residents reported increased knowledge of community resources and breastfeeding techniques they can incorporate into their clinics. Scheduling conflicts and clarified expectations of home visit goals will need to be addressed to develop this program further.

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CAN WE IMPROVE PHYSICIAN KNOWLEDGE ABOUT MANAGING ENVIRONMENTAL TRIGGERS OF ASTHMA?

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Purpose of Study: Environmental exposures can exacerbate asthma and control of these triggers is beneficial to patients. The purpose of the study is to determine if educating pediatricians about environmental triggers of asthma increases their knowledge and improves their attitudes for asthma treatment.

Methods Used: A 1-hour presentation, based on the available scientific evidence of the management of environmental triggers for asthma, was delivered to pediatricians and pediatric residents. Prior to the educational intervention, survey data was collected on participants. Questions included knowledge of environmental triggers of asthma, practices of environmental history taking, and advice given to patients about environmental trigger reduction. Knowledge and practice items were repeated after the intervention. Data were entered into SPSS and frequency distributions were calculated. Pre and post data were analyzed using paired t-tests.

Summary of Results: Pre and post data were collected on 46 participants. At baseline, physicians reported having an expert or very good knowledge of the following environmental triggers: dust mites 26.1%, tobacco smoke 63.0%, animal allergens 45.7%, cockroach 32.6%, molds 30.4%, and outdoor air pollution 21.7%. Physicians were likely to ask patients or parents about the following exposures all of the time: dust mites 8.7% (pre-test) v. 41.3% (post-test), tobacco smoke 60.9% (pre) v. 78.3% (post), animal allergens 23.9% (pre) v. 52.2 % (post), cockroach exposure 6.5% (pre) v. 37.0% (post), mold exposure 8.7 % (pre) v. 39.1% (post), outdoor air pollution 2.2% (pre) v. 30.4% (post), wood smoke 6.5% (pre) v. 30.4% (post), and outdoor pollution 8.7% (pre) v. 34.8% (post). Physicians were likely to recommend the following interventions to patients all of the time: dust mite covers 6.5% v. 45.7%, advise family to stop smoking 58.7% v. 71.7%, refer patients to an asthma specialist 6.5% v. 21.7%, and advise patients about other ways to decrease second hand smoke exposure 32.6% v. 58.7%. All of the above differences were statistically significant.

Conclusions: Pediatricians and pediatric residents reported improved knowledge about environmental triggers and appeared more likely to advise patients about environmental trigger reduction.

Perinatal Medicine I

Concurrent Session

2:00 PM

Friday, February 26, 2010

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CXCR2 LIGANDS RECRUIT MACROPHAGES TO THE INTESTINAL MUCOSA DURING NECROTIZING ENTEROCOLITIS

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Purpose of Study: NEC is characterized by increased infiltration with activated macrophages in the intestine. We have shown recently that intestinal macrophages are incapable of clonal expansion and that gut macrophage pool can expand only via recruitment of differentiating monocytes. In this study, we investigated whether monocytes are recruited to the intestine during NEC due to increased epithelial expression of chemokines.

Methods Used: HAM56+ macrophages were enumerated in premature human intestinal tissues with NEC, no intestinal disease, and in healed NEC (ostomy repair) (n = 3–5 each). We then used an established rat model of NEC (n = 40; fed rat milk substitute, subjected to hypothermia & hypoxia q12 hrs). Using IHC, we then enumerated CD11b+ CD68+ macrophages/villus in animals with NEC and in dam-fed controls. The expression of 28 chemo-attractants known to recruit macrophage precursors was measured by qPCR and confirmed by western blots/IHC. We then used rat monocytes in a fluorescence-based chemotaxis assay to measure chemotactic activity of tissue lysates.

Summary of Results: Human NEC was marked by increased lamina propria macrophages (normal premature: 20±6/villus, acute NEC: 56±8/villus, healed NEC: 33±7/villus; p < 0.01), which display an activated morphology and express inflammatory cytokines (TNF-α). Macrophages were also increased 3.5–4x in our rat model of NEC. In our qPCR array, we identified a >2-fold increase in expression of CXCL2, CXCL5, CCL2, CCL3, CCL19, and CCL25, where CXCL5 and CXCL2 were most-highly upregulated. Increased CXCL5 and CXCL2 expression was confirmed in rat NEC tissue by immunohistochemistry and western blots, and these data were further validated in archived human tissue. Lysates of intestinal tissue from pups with NEC showed strong chemotactic activity for monocytes, which was blocked by anti-CXCR2 antibodies and by SB225190, a specific inhibitor of CXCR2.

Conclusions: NEC is associated with a marked increase in lamina propria macrophages, an effect mediated via increased epithelial expression of CXCR2 ligands, CXCL5 and CXCL2. These findings are of potential therapeutic interest as several pharmacological inhibitors of CXCR2 are currently in early clinical trials.

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EARLY INTRODUCTION OF NON-PATHOGENIC BACTERIA PROMOTES VILLUS DEVELOPMENT IN GERM-FREE MICE BY RECRUITING DENDRITIC CELLS TO THE LAMINA PROPRIA

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Purpose of Study: Gut bacterial colonization is frequently delayed in preterm infants because of delayed enteral feedings and the use of antibiotics. This 'germ-free' state is presumed to alter the morphological/functional development of the gut mucosa. We used germ-free (GF) mice to determine whether early introduction of a limited, well-defined set of non-pathogenic bacteria could correct the morphological abnormalities of the GF mucosa.

Methods Used: We compared conventionally-reared (CR), germ-free (GF), and GF mice colonized on postnatal day 2 with altered Schaedler's flora (ASF; 8 well-defined bacteria: 2 lactobacilli, 1 Bacteroides, 3 Clostridia, 1 Flexistipes and 1 unidentified spp.). Mice were euthanized at 3–4 and 10–12 wks of age and computer-assisted measurements of the villi, lamina propria (LP), crypts, and intestinal epithelial cells (IEC) were made. LP cells were defined by immunostaining (IHC) and FACS. Dendritic cell (DC) chemokine expression was measured by qPCR, western blots, and IHC. DC chemotaxis to epithelial-conditioned media (E-CMs) was measured in vitro using a fluorescence-based assay.

Summary of Results: Villi in GF mice were slender, finger-like in shape, which contrasted with larger, lanceolate villi in CR animals; major differences were in LP area (CR 14251 ± 1267 vs. GF $5134 \pm 850 \mu\text{m}^2$, $p < 0.05$) and LP cells (CR 83 ± 9 and GF 29 ± 2 cells/villus, $p < 0.05$) but not in IEC parameters. In ASF mice, villus area, LP area, and the number of LP cells were partially restored. ASF mice had increased CD11c+ cells in the LP, most of which were CD11b+ CD11c(hi) myeloid DCs. We identified increased expression of CCL20 in ASF intestinal epithelium; E-CMs from ASF intestine showed strong chemotactic activity for myeloid DCs (isolated from tissue by immunoselection), which was blocked by anti-CCL20 antibodies.

Conclusions: (1) Introduction of non-pathogenic bacteria can restore villus architecture in the GF intestine; (2) besides direct effects on IECs, "trophic" effects of gut microflora on villus development may involve expansion of LP cell populations in the villus core; (2) introduction of limited bacterial ecosystems may alter leukocyte populations in the lamina propria, potentially affecting mucosal inflammatory responses.

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DECREASED EXPRESSION OF TGF- β RECEPTORS DURING NEC MAY SENSITIZE INTESTINAL MACROPHAGES TO BACTERIAL PRODUCTS AND AUGMENT MUCOSAL INFLAMMATION

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Purpose of Study: We have shown that TGF- β plays an important role in the normal downregulation of inflammatory properties of intestinal macrophages and that developmental deficiency of TGF- β 2 expression in intestine may predispose preterm infants to necrotizing enterocolitis (NEC). In this study, we investigated whether NEC is also associated with reduced intestinal expression of TGF- β receptors and consequent loss of TGF- β -induced signaling, which may further sensitize intestinal macrophages to bacterial products.

Methods Used: TGF- β receptor I (TBR I) and TBR II immunoreactivity was compared in archived tissue samples of human NEC and matched controls. To investigate the effects of reduced TGF- β receptor expression, we used a conditional knock-out mouse where Zn supplementation induces a dominant-negative, kinase-defective mutant TBR II transgene (DNIIR) that blocks TBR II expression and TGF- β signaling. Bone marrow-derived macrophages were prepared from wild type (WT) and DNIIR mice by culturing myeloid precursors for 7 days in the presence of M-CSF and $25 \mu\text{M}$ ZnCl₂. LPS-induced macrophage cytokine production and expression of mediators in TLR4- and NF- κ B-activated pathways was measured using focused qPCR arrays, and then confirmed on intestinal macrophages in vivo by IHC after intraperitoneal LPS (1 mg/kg) administration.

Summary of Results: NEC was associated with a marked reduction in TBR I and TBR II expression. Macrophages from DNIIR mice showed a 2-15x greater cytokine response following LPS stimulation than cells from WT mice. These effects were most prominent for IL-6 and MIP-2/CXCL2. Strong MIP-2 immunoreactivity was detected in intestinal macrophages in LPS-treated DNIIR but not WT mice. Macrophages in DNIIR mice showed increased expression of TLR4, Myd88, IRAK1, TAK1, IKK α , and NF- κ B2 in the TLR4- and NF- κ B-activated signaling pathways.

Conclusions: (1) Decreased expression of TGF- β receptors during NEC may sensitize intestinal macrophages to bacterial products and augment mucosal inflammation; (2) Increased sensitivity of TBR II-deficient macrophages to LPS can be explained by the upregulation of key rate-limiting mediators in the TLR4- and NF- κ B-activated signaling pathways.

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BACTERIAL COLONIZATION MAY INFLUENCE TIGHT JUNCTION EXPRESSION IN THE DEVELOPING MURINE INTESTINE

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Purpose of Study: Necrotizing Enterocolitis (NEC) is a leading cause of neonatal morbidity and mortality that predominately affects preterm infants.

Although the exact etiology of NEC is unknown, immature intestinal barrier function and abnormal bacterial colonization are implicated in its pathogenesis. Tight junctions (TJ) are a vital component of the intestinal barrier and its regulation of intestinal permeability. However, little is known about how bacterial colonization may influence TJ development in the immature developing intestine.

Methods Used: Using a mouse model of immature intestine, we screened 29 TJ proteins by qRT-PCR to identify temporal changes in expression in the developing ileum. Candidate TJ proteins were further analyzed by immunoblot (IB) and immunofluorescent microscopy (IF). To determine the role of bacterial colonization and toll-like receptor (TLR) signaling in regulating TJ protein expression, we compared results of control mice to antibiotic-treated and MyD88 null mice, respectively.

Summary of Results: Tight junction expression demonstrates two patterns of changes from the immediate postnatal period to the more mature adult intestine. Most TJ proteins demonstrate decreasing expression over time. However, several TJ proteins including Claudin-3, Claudin-7, and Claudin-15 demonstrate peak expression at 3 weeks which temporally correlates with major changes in intestinal bacterial colonization. Preliminary data indicates that these changes are not regulated by commensal bacterial signaling through TLRs.

Conclusions: We have identified several TJ proteins with peak expression at 3 weeks of murine life, a period which follows the acquisition of lactobacilli and other gut flora. Commensal bacterial colonization may drive these changes. Further studies investigating how commensal bacteria regulate these changes may provide insight into how abnormal and normal bacterial colonization may influence intestinal barrier function and thus predisposition to NEC in the premature infant.

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HYPEROSMOLAR FEEDINGS IN THE NICU: AN UNDERAPPRECIATED CAUSE OF MORBIDITY?

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Purpose of Study: The objective of this study was to measure the osmolality of common milk-medication mixtures used in the intensive care nursery and compare to recommendations from the American Academy of Pediatrics (AAP).

Methods Used: Volumes of infant formula and pooled human milk samples were chosen to represent a single feeding volume in a 1 kilogram baby. Doses of medications were determined from NeoFax®. The osmolalities of milk alone as well as milk-medication mixtures were measured in triplicate by freezing point depression.

Summary of Results: Six types of milk (formula and human milk) and 10 commonly used medications were tested either 1 in 1 (1 drug in 1 volume of milk) or in combinations (more than 1 medication in a single milk volume). The addition of liquid vitamin drops alone resulted in milk osmolalities approaching 1,000 mOsm/kg H₂O, well above the AAP recommended limit of 480. When mixtures of several medications in milk were tested, osmolalities ranged from 1,000 to over 1,500. Multiple additives to elemental formula, already high in osmolality and commonly used in infants with compromised gastrointestinal tracts, resulted in osmolalities of nearly 2,000. Diuretics, vitamin drops and phenobarbital, specifically, raised osmolalities the most.

Conclusions: When using milk/formula as a vehicle for the administration of oral medications, healthcare professionals need to be mindful of the potential osmotic effects of such mixtures. When possible, administration times should be spaced in such a way that as few medications as possible can be given at the same time.

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TRANSFUSION INDUCED GUT AND RENAL ISCHEMIA CORRELATES WITH PROLONGED RED CELL STORAGE

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Purpose of Study: Storage of PRBCs, and the so called "storage lesion" is thought to be a potential concern in the development of "post transfusion" NEC in the preterm infant. The pathological effect of storage induced red cell hemolysis on endothelial cell function may alter the regulation of vascular tone leading to ischemia of different tissue beds. Our study examined the

hypothesis that the length of time PRBCs are stored directly correlates with a higher incidence in tissue perfusion changes, leading to increased risk for tissue damage.

Methods Used: Yorkshire Duroc commercial piglets weighing 1.5–2.5 kg were used to evaluate the near infrared spectroscopy (NIRS) changes in regional oxygen saturation of the brain, kidney, and abdominal organs before, during and after PRBC transfusion. Piglet PRBC's were stored for 5–7, 10–14, and 20–23 days prior to transfusion. NIRS recordings were correlated to real time vital signs and laboratory studies. Blood samples were collected prior to, during and every hour post transfusion for quantification of inflammatory markers and coagulation cascade activation. Tissue histology and gross exam was performed at autopsy immediately after the experiment.

Summary of Results: 1) Severity of gut and renal perfusion changes increased with increasing length of PRBC storage. Perfusion changes were minimal in the cerebral vascular bed. 2) At autopsy, spontaneous perforations were noted in the ileal cecal area in 1 of 4 piglets in the 10–14 day epoch, and in 1 of 4 piglets in the 20–23 day epoch. All animals examined at 10–14 and 20–23 days of PRBC storage demonstrated gross and microscopic ischemic changes in the intestine. 3) Negative effects of prolonged red cell storage on tissue perfusion could be reduced by limiting transfusion volume to less than 8ml/kg.

Conclusions: Our results suggest that prolonged red cell storage negatively impacts tissue perfusion leading to gut and renal ischemia in the newborn piglet. Ongoing studies investigating potential effects of prolonged red cell storage on tissue perfusion in the preterm infant may lead to changes in clinical practice. Determining how to administer and monitor for transfusion associated tissue bed perfusion changes may be able to reduce potentially devastating complications such as NEC.

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THE INFLUENCE OF PASTEURIZATION AND TIMING OF BREAST MILK COLLECTION ON LACTOFERRIN AND CYTOKINE CONCENTRATION

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Purpose of Study: Maternal breast milk (MBM) decreases the incidence of necrotizing enterocolitis (NEC). Lactoferrin (LF) and cytokines (IL-10, IL-6) are postulated to play a role in the protective effects of MBM for NEC. Pasteurized human donor breast milk (DBM) is used in many neonatal intensive care units to feed premature infants when MBM is not available. DBM has less immunoglobulin and lysozyme concentrations than MBM; however, the content of LF and cytokines has yet to be characterized. In this study, we determined if LF, IL-6 and IL-10 levels are affected by timing of MBM collection (hrs after birth and/or gestational age) and BM pasteurization.

Methods Used: After informed consent, expressed MBM samples were collected from randomly selected mothers delivering at University Hospital in San Antonio, TX and classified according to both time of collection (early, <48 hrs or late, >48 hrs following birth) and gestation (preterm vs. term). Samples were aliquoted, centrifuged and whey was isolated and stored at -80° . DBM samples were obtained from nursery supply and treated in the same manner. Western blotting was performed with recombinant human LF and formula as controls. Concentrations of LF, IL-6 and IL-10 were determined using commercial ELISA (R&D Systems, Minneapolis, MN). Significance was determined using ANOVA (SPSS 11.5).

Summary of Results: A total of 80 samples were obtained. Lactoferrin protein content was significantly decreased in DBM when compared to MBM ($p < 0.05$). In addition, DBM had lower LF, IL6 and IL-10 concentrations than MBM regardless of time of collection or gestation ($p < 0.05$). Lactoferrin and IL-6 concentrations in MBM were unaffected by time of collection or gestation. Late preterm MBM had significantly lower levels of IL-10 when compared to late term MBM (8.9 ± 5.9 pg/ml vs. 45.0 ± 42.3 pg/ml, $p < 0.05$).

Conclusions: LF, IL-6 and IL-10 levels were lower in DBM as compared to MBM, suggesting that pasteurization adversely affects known beneficial components of MBM. Interestingly, IL-10 levels were significantly lower in preterm MBM than term MBM. Further studies investigating the role of variations in LF and cytokine levels in MBM and the incidence of NEC in premature infants are ongoing.

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CORTICOSTEROID (CS) RESPONSES FOLLOWING HYPOXIC PRECONDITIONING (PC) PROVIDE NEUROPROTECTION AGAINST SUBSEQUENT HYPOXIC-ISCHEMIC (HI) BRAIN INJURY IN NEWBORN RATS

AJ. Bhatt, Y. Feng, PG. Rhodes *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: In newborn animals, PC stress induced by mild hypoxia results in adaptive responses which provide sizeable protection against subsequent severe HI brain injury. Limited research has evaluated the hormonal response of an up-regulation of CS following PC. Our objectives were to evaluate CS changes following hypoxic PC and their neuroprotective effects against HI brain injury in newborn rats.

Methods Used: To measure, CS response to hypoxic PC, plasma corticosterone levels were measured in 6 d old newborn rats in naïve, sham ($21\% \text{ O}_2 \times 3\text{h}$) and hypoxic PC ($8\% \text{ O}_2 \times 3\text{h}$) groups. To investigate the role of the CS response in hypoxic PC induced neuroprotection, on postnatal day (P) 6, rat pups from each litter were culled to 12 newborn and randomly divided into three groups (NoPC+HI, Veh+PC+HI, RU486+PC+HI). Fifteen minutes prior to PC, rat pups in the Veh+PC+HI and RU486+PC+HI groups received vehicle or glucocorticoid receptor (GR) blocker (RU486, 60 mg/kg) s.c., respectively. Afterwards, all rat pups were exposed to normoxia (NoPC+HI) or hypoxia (Veh+PC+HI, RU486+PC+HI) for 3 h and then after 24 h had the right carotid artery permanently ligated followed by 140 min of hypoxia ($8\% \text{ O}_2$) at d 7 (HI). Brains from rat pups at the corresponding age without any exposure to PC or HI or drug were examined for comparison (Sham).

Summary of Results: Following hypoxic PC, plasma corticosterone levels were increased at 30 mins with a peak at 1 h (~ 11 fold) and returned to baseline at 2 h compared to naïve and sham groups ($n = 2-6/\text{group}$, $p < 0.01$). RU 486 treatment before the PC significantly inhibited the PC induced fall in increase in caspase-3 activity (24 h), water content percentage (24 h) and microscopic brain damage measured by histo-pathological score (72 h after HI) in the ipsilateral hemisphere following HI ($n = 6-10/\text{group}$, $p < 0.01$ to < 0.05).

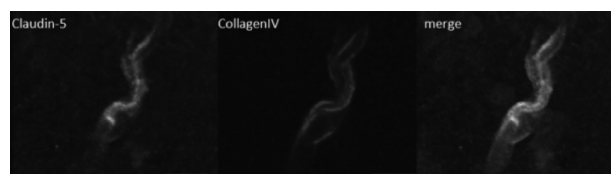
Conclusions: We conclude that the pituitary-adrenal axis responds immediately and robustly to hypoxic PC and plays a role in the neuroprotection against HI in newborn rats. Further studies will quantify GR blocker induced changes in the delayed neuroprotection by hypoxic PC using a gross brain damage score and the percent loss of the ipsilateral hemispheric weight measured at 22 d following HI.

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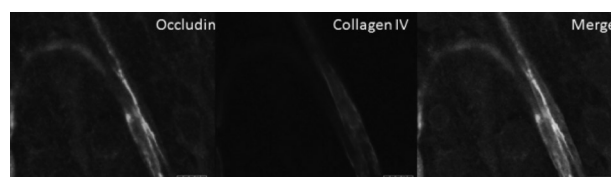
QUANTIFICATION AND DISTRIBUTION OF TIGHT JUNCTION PROTEINS IN THE DEVELOPING RAT BRAIN

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Purpose of Study: To describe the distribution and level of expression of cerebral tight junction proteins (TJPs) occludin and claudin-5 in the rat



Immunofluorescence shows claudin-5 distribution in a P7 BBB rat cortex.



Immunofluorescence shows occludin distribution in a P7 BBB rat cortex.

brain during development. Although occludin and claudin-5 are commonly used as biomarkers to study function of the BBB in the immature rat brain, the role of these proteins in BBB function has not been clearly elucidated.

Methods Used: Brain protein expression was determined with Western immunoblotting (WB) and enzyme-linked immunosorbent assay (ELISA). Immunofluorescence was used to determine distribution of TJPs in the rat BBB at different times of development; E17 (embryo at 80% of gestation), P7 (postnatal day 7) and P70 (postnatal day 70). Level of protein expression was compared with analysis of variance (ANOVA).

Summary of Results: WB showed clear expression of claudin-5 and occludin in the rat brain from embryonic age. Occludin expression as measured by ELISA showed the P7 group was significantly higher than the E17 group ($p < 0.05$). Immunofluorescence demonstrated that claudin-5 and occludin were localized in the BBB at P7. Detection of occludin proved to be more robust when compared with claudin-5.

Conclusions: In this study, claudin-5 expression increased with developmental age. Interestingly, occludin followed a differential pattern of expression and was highest in the P7 rat. The expression of these TJPs was correlated with their distribution within the BBB. The differential expression of TJPs during development may lead to speculation about their relative importance to BBB function in the immature brain. Perhaps occludin may play a greater role in BBB formation in the immature brain while claudin-5 is essential for maintenance of the BBB in the mature brain.

Renal, Electrolyte and Hypertension I Concurrent Session

2:00 PM

Friday, February 26, 2010

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ANGIOTENSIN (ANG) II STIMULATES PAPILLOGENESIS DURING LATE METANEPHRIC DEVELOPMENT

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Purpose of Study: Branching morphogenesis of the ureteric bud (UB) is a key developmental process which gives rise to the ureter, pelvis, calyces and collecting ducts. We recently reported that Ang II, acting via the AT1R receptor (AT1R), stimulates UB branching morphogenesis during early stages of metanephric development (Yosypiv et al. *Kidney International*, 2008). In the present study, we tested the hypothesis that aberrant AT1R signaling impairs papillary morphogenesis during later stages of metanephric development.

Methods Used: We first examined the effect of genetic inactivation of subtype A of AT1R (AT1AR) in mice on papillary growth on postnatal (P) day P1. To determine whether Ang II AT1R directly stimulates papillary morphogenesis, we next examined the effect of the specific AT1R antagonist, candesartan, on papillary growth using ex vivo papillary culture. Papillas were dissected from Hoxb7-GFP+ mouse metanephroi on P2 and grown in 3-dimensional collagen matrix gels located on air-fluid interface in the presence of media (control, $n=3$) or candesartan (10^{-6} M, $n=3$) for 48 hours. Images were acquired at time of dissection ("0" hours), 24 and 48 hours by time-lapse microscopy. Papillary area was determined at every time point by Slide book 4.0 image processing software and percent change in papillary area relatively to time "0" was compared between the groups.

Summary of Results: P1 AT1AR-/- metanephroi exhibited a smaller papilla compared with AT1AR+/+ neonatal kidneys. Treatment with candesartan decreased papillary area after 48 hours of culture (77 ± 6.6 vs. $100 \pm 0\%$, $p < 0.05$). In contrast, papillary area in control group at 48 hours did not differ from baseline (93 ± 12 vs. $100 \pm 0\%$, $p = 0.6$). The results demonstrate that lack of AT1AR in mice results in abnormal papillary development. Moreover, antagonism of the AT1R directly inhibits growth of neonatal papillas grown ex vivo.

Conclusions: We conclude that Ang II, acting via the AT1R, stimulates papillogenesis during late metanephric development. These findings support the hypothesis that abnormal collecting system development in RAS-deficient mice is due, in part, to aberrant collecting duct growth.

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DEVELOPMENTAL TISSUE-SPECIFIC EXPRESSION OF THE PRORENIN RECEPTOR

R. Song, S. Baranovic, C. Garrett, IV. Yosypiv *Tulane University, New Orleans, LA.*

Purpose of Study: The prorenin receptor [(P)RR] has two major roles: 1) Mediate specific intracellular effects of prorenin and renin and 2) Enhance their enzymatic activity on the plasma membrane. This study examined (P)RR gene and protein expression during mouse organogenesis.

Methods Used: (P)RR mRNA levels were determined in the brain, kidney, lung and heart of CD1 mice on embryonic (E) days E12.5-18.5 and postnatal (P) days P1, P10 and P60 (adult) by quantitative RT-PCR. Cellular distribution of the PRR protein in the metanephros was mapped by immunohistochemistry and of (P)RR mRNA- by in situ hybridization (ISH).

Summary of Results: RT-PCR demonstrated that brain (P)RR mRNA levels are low initially, increase on E16.5 and remain unchanged thereafter until adulthood. Kidney (P)RR mRNA levels increase progressively during gestation, remain unchanged on P1, increase on P10 and decline in adulthood. Lung (P)RR mRNA abundance increases progressively during gestation, peaks on P10 and remains high in adulthood. In the heart, (P)RR mRNA contents remain stable during gestation to subsequently decrease on P10 and P60. The (P)RR protein is weakly expressed in the developing metanephros in inner tubular structures as early as on E14.5. On E16.5 and E18.5, (P)RR is present in the ureteric bud (UB) epithelia followed by glomerular mesangium. On P1 and P10, (P)RR is most abundant on the luminal aspect of collecting ducts followed by proximal tubules and mesangium. This expression pattern persists into adulthood. ISH revealed weak diffuse presence of (P)RR mRNA in the inner mesenchyme and UBs on E13.5. A significant increase in the intensity of (P)RR mRNA expression throughout the kidney was observed on E14.5.

Conclusions: In summary, (P)RR mRNA expression increases with maturation in the brain, lung and kidney and decreases in the heart. (P)RR protein expression increases progressively during metanephric development. Spatially, (P)RR protein is restricted to UBs/collecting ducts followed by glomerular mesangium and tubules. During early metanephric development, (P)RR mRNA is broadly localized in the mesenchyme and UB epithelia. These results demonstrate that (P)RR gene is developmentally regulated in a tissue-specific manner. The enrichment of (P)RR in renal tubules and glomeruli suggests a novel function for the (P)RR in the regulation of nephron development.

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CINOBUFATALIN INDUCES THE SYNDROME OF PREECLAMPSIA IN A RAT MODEL

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Purpose of Study: Investigate the effect of cinobufatalin on rat pregnancy. Preeclampsia is a hypertensive disorder of pregnancy. Increased levels of marinobufagenin (MBG), an endogenous inhibitor of the Na⁺/K⁺ ATPase, is associated with hypertension, proteinuria and intrauterine growth restriction (IUGR) in the rat. MBG impairs cytotrophoblast (CTB) functions critical for placental development. Cinobufatalin (CBT) is an analogue of MBG and also inhibits Na⁺/K⁺ ATPase.

Methods Used: Five groups of animals were studied: control; nonpregnant (C, $n = 10$); normal pregnant (NP, $n = 10$); pregnant rats which received injections of desoxycorticosterone acetate and 0.9% saline as their drinking water (PDS, $n = 10$); normal pregnant rats injected with CBT ($7.65 \mu\text{g/kg/d}$, NPC, $n = 10$) and normal pregnant rats injected with MBG ($7.65 \mu\text{g/kg/d}$, NPM, $n = 8$).

Summary of Results: Blood pressure (BP) in the control (C) did not change over the course of the experiments (18–20 days) but mean BP decreased significantly in the NP group: C: $104 \pm 5 \text{ mmHg}$ to $102 \pm 4 \text{ mmHg}$ ($p = \text{NS}$); NP group: $105 \pm 4 \text{ mmHg}$ to $90 \pm 6 \text{ mmHg}$ ($p < 0.05$). BP increased significantly from baseline in the PDS, NPC and NPM groups ($p < 0.05$): PDS: $103 \pm 7 \text{ mmHg}$ to $140 \pm 8 \text{ mmHg}$; NPC group: $103 \pm 3 \text{ mmHg}$ to $128 \pm 6 \text{ mmHg}$ and NPM group: $108 \pm 7 \text{ mmHg}$ to $132 \pm 6 \text{ mmHg}$. Final BP differed from those obtained in the control and NP group ($p < 0.05$). The PDS, NPC and NPM animals showed a statistically significant increase in protein excretion when compared with the control and NP groups ($p < 0.05$): C:

1.1±0.9 mg/24hr; NP: 2.4 ± 1.2 mg/24hr; PDS: 5.6 ± 1.8 mg/24hr; NPC 5.8±1.8 mg/24hr; NPM 4.8±1.6 mg/24hr. Creatinine clearance was not different among the NP, PDS, NPC and NPM groups but was significantly increased from the control group ($p<0.05$): C: 0.40±0.12 ml/min; NP: 0.91±0.18 ml/min; PDS: 1.03±0.23 ml/min; NPC: 1.05±0.25 ml/min; NPM: 1.01±0.12 ml/min. Regarding IUGR, the number of pups per liter was significantly lower in PDS, NPC and NPM groups compared to NP group ($p<0.05$): NP 15.0±1.9, PDS 11.1±1.4, NPC 12.2±1.8 and NPM 12.2±1.7. The percentage of malformed fetuses was significantly higher in the PDS, NPC and NPM groups compared to the NP group ($p<0.05$): NP 0, PDS 18.0, NPC 11.0 and NPM 6.0.

Conclusions: CBT, a bufadienolide similar in structure to MBG, induces the characteristics of preeclampsia in rats similar to MBG.

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FAMILIAL INTERSTITIAL NEPHRITIS - A LINKAGE STUDY

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Purpose of Study: Chronic tubulo-interstitial nephritis (TIN) leads to progressive decline in renal function, involving patho-physiological processes that are implicated in the progression of most types of renal disease. Hereditary Interstitial Nephritis is seen in the setting of autosomal dominant medullary cystic kidney disease (MCKD) and nephronophthisis. This study sought to define a new entity, Familial Interstitial Nephritis without features of medullary cystic kidney disease or nephrocystic disease and to seek evidence of linkage of this disease to a genetic locus.

Methods Used: Affected individuals were initially identified by the Department of Nephrology, Beaumont Hospital, Ireland. Affected families had two or more members with biopsy-proven primary TIN in the absence of renal cysts or hyperuricemia. All family members were offered screening to determine their affection status by measurement of serum creatinine, serum uric acid levels and qualitative urinalysis. Genomic DNA was isolated from blood using a standardized salting out procedure. The maximal attainable logarithm of the odds (LOD) scores for each pedigree, using full pedigree and affected-only models, was calculated via computer simulation with the SIMLINK 4.1 program. Genome wide linkage scan was performed with the Illumina Infinium II HumanLinkage-12 genotyping beadchip. Two-point and parametric multi-point LOD scores were calculated by using the VITESSE statistical program.

Summary of Results: Six families with 32 affected individuals were identified from medical records and subsequent family screening. Four of these had an autosomal dominant inheritance pattern. The largest kindred, with 12 affected individuals spanning 3 generations, had a maximal predicted LOD score of 4.5 when calculated with SIMLINK. There were a number of areas with suggestive linkage to a disease locus with LOD scores between 1.5 and 2.5 located at Chromosomes 1p, 1q, 2q, 3q, 8q and 11q.

Conclusions: Interstitial Nephritis may be inherited in autosomal dominant fashion. The kindreds described here do not have renal cysts or hyperuricemia. Whether they represent isolated interstitial nephritis or fall within the spectrum of MCKD is to be determined. Further genetic information and study will be required to establish or disprove linkage in the above areas.

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THE EPIGENETIC HISTONE CODE OF THE DEVELOPING NEPHRON

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Purpose of Study: Mesenchyme-to-epithelium transition of Six2+ cells forms a polarized epithelial progenitor, renal vesicle, which gives rise to the nephron. Epigenetic memory is a driving force in cell fate determination. Thus, we hypothesize that Six2-derived nephron progenitors retain, gain or lose epigenetic marks, and that successive stages of nephrogenesis are marked by distinct cassettes of combinatorial epigenetic modifications.

Methods Used: Embryonic kidney sections (E15.5) were probed with antibodies against histone modifications or modifying enzymes and markers of differentiation. Z-plane images (>15) were acquired, deconvolved and colocalization determined.

Summary of Results: Six2+ cells exhibited a wide range of epigenetic modifications including activating (H3K4/36me3, H4R3me2, H3R17me2) and repressive (H3K9/27me3) marks. During transition to RV, Six2 is repressed and Lhx1 is expressed de novo with a concomitant loss of both

lysine and arginine methylation (H3K4/9/79me2, H3K9/27/36me3, H3R17me2, H4R3me2), with the exception of H3K4me3 and acquisition of H3K4me1 and H3K79me3. Next, the responsible methyltransferases (KMT) and demethylases (KDM) were examined. Specifically, Ash2L/LSD1 (H3K4 KMT/KDM), Suvh39 (H3K9 KMT), Ezh1/2 (H3K27 KMT) and Dot1 (H3K79 KMT) were examined. Ash2L/H3K4me3 were present in epithelial nephron progenitors similar to the transcription factor Pax2, whereas Lsd1 was most pronounced in the mesenchyme. Suvh39/H3K9me3 were present in the cap mesenchyme, as was the H3K79 methyltransferase Dot1, though H3K79/Dot1 positive cells were also seen in the more mature collecting system. Interestingly, Ezh1 and Ezh2 showed differential expression in cortical cells dorsal to Six2+ cells and Six2+ cells, respectively.

Conclusions: Renal progenitors express both activator and repressor marks, consistent with the "binary mark" observed in other progenitor cell populations. Differentiation is accompanied by loss of some marks (i.e. H4R3me2, H3K9me3) as well as the gain of others (i.e. H3K79me3, H3K27me3). Importantly, the histone modifying enzymes investigated demonstrate a more compartmentalized expression, suggesting that epigenetic regulation is integral to nephrogenesis. Finally, the differential and combinatorial expression of histone modifications and enzymes provides a platform to examine the epigenetic regulation of key nephrogenic genes.

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A LOWER ACID-INDUCING DIET LOWERS AUGMENTED ACID RETENTION ASSOCIATED WITH REDUCED GFR

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Purpose of Study: Increased acid retention (AR) associated with reduced GFR mediates GFR decline in some animal models. We explored if 1) subjects with reduced GFR have increased AR, and 2) whether a lower acid-inducing diet reduces AR. Our hypothesis was that patients with greater AR would have smaller reductions in 8 hour NAE (net acid excretion) after NaHCO₃ bolus, reflecting a greater titration of administered NaHCO₃.

Methods Used: We compared AR as measured by 8h NAE after a 0.5 meq/Kg bw oral NaHCO₃ bolus in subjects with hypertensive nephropathy eating ad lib and after reducing dietary potential renal acid load (PRAL) by adding fruits/vegetables for 30 days. We also measured serum total CO₂ (TCO₂) to assess retained intact NaHCO₃. Subjects were grouped according to MDRDS-estimated GFR (eGFR): >90ml/min, N=26; 60-90 ml/min, N=40; 30-59 ml/min, N=36; and 15-29 ml/min, N=36. Measures were compared between groups with ANOVA and Tukey's post hoc comparisons and changes within each GFR group were assessed with one-sample t tests.

Summary of Results: When eating ad lib, post-NaHCO₃ bolus 8h NAE (meq, means ± SD) was statistically significantly higher in eGFR 15-29 ml/min than 30-59 ml/min (24.2 ± 1.2 vs. 20.7 ± 2.0, $p = 0.0001$), higher in 30-59 ml/min than 60-90 ml/min (18.2 ± 5.1, $p = 0.007$), and higher in 60-90 ml/min than >90 ml/min (9.5 ± 3.4, $p < 0.0001$). Serum TCO₂ was not higher in the low eGFR groups than in >90 ml/min group, consistent with higher AR rather than higher retention of intact HCO₃ in subjects with lower eGFR. After diet intervention and post NaHCO₃ bolus 8h NAE was significantly lower in each of the eGFR groups ($p < 0.0001$) except the >90 ml/min group (9.8 ± 3.9 vs. 9.5 ± 3.4, $p = 0.52$), consistent with reduced AR in the low eGFR but not normal eGFR group. PRAL was not statistically different among eGFR groups at baseline but diet intervention reduced PRAL significantly in all eGFR groups ($p < 0.0001$).

Conclusions: Subjects with reduced eGFR have increased AR that is reduced by adding fruits/vegetables to their ad lib diets. These data support testing this dietary intervention as a kidney protective strategy in subjects with hypertensive and possibly other nephropathies.

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A LOWER ACID-INDUCING DIET LOWERS AUGMENTED KIDNEY ENDOTHELIN PRODUCTION ASSOCIATED WITH REDUCED GFR

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Purpose of Study: Increased endothelin activity associated with metabolic acidosis and/or increased intrinsic acid production mediates GFR decline in

some animal models. We tested the hypothesis that a lower acid-inducing diet reduces urine endothelin-1 excretion (UET-1V), a surrogate of kidney endothelin production.

Methods Used: We measured UET-1V, dietary potential renal acid load (PRAL), and 8 hour urine net acid excretion (8h NAE) in subjects with hypertensive nephropathy grouped according to MDRDS-estimated GFR (eGFR): >90ml/min, N=26; 60-90ml/min, N= 40; 30-59 ml/min, N=36; and 15-29 ml/min, N=36. Parameters were measured at baseline and after 30 days of a diet intervention of fruits/vegetables. Measures were compared between groups with ANOVA with Tukey's post hoc comparisons and within each GFR group with one-sample t test.

Summary of Results: Baseline UET-1V was statistically significantly different between eGFR groups and was highest in the lowest eGFR group and lowest in the group with eGFR >90 ml/min (overall $p < 0.0001$). The UET-1V (ng/g creatinine, mean $\pm$ SD) measured after diet intervention, as compared to baseline, was significantly lower in eGFR groups 15-29 ml/min (6.9 ± 2.4 vs. 7.6 ± 2.9 , respectively, $p < 0.0001$), 30-59 ml/min (5.7 ± 1.7 vs. 6.2 ± 2.1 , respectively, $p=0.0005$), and 60-90 ml/min (5.0 ± 1.0 vs. 5.5 ± 1.2 , respectively, $p=0.0006$) but not in the >90 ml/min group (3.3 ± 1.2 vs. 3.5 ± 1.7 respectively, $p=0.34$). PRAL and 8h NAE were not statistically different among eGFR groups at baseline but the dietary intervention lowered PRAL and 8h NAE in each eGFR group ($p < 0.0001$). The effect of the dietary intervention on PRAL and 8h NAE did not vary by eGFR group.

Conclusions: Subjects with reduced GFR due to hypertensive nephropathy have increased UET-1V, consistent with increased kidney endothelin production. Lowering dietary PRAL by adding fruits and vegetables lowers UET-1V in these subjects with reduced but not normal GFR. These data support testing this dietary intervention as a kidney protective strategy in subjects with hypertensive and possibly other nephropathies.

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HEME OXYGENASE-1 EXPRESSION REGULATES IMMUNE CELL INFILTRATION IN RENAL INFLAMMATION

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Purpose of Study: Heme oxygenase-1 (HO-1) modulates innate and adaptive immune responses. Infiltration of macrophages and dendritic cells (DC's) following unilateral ureteral obstruction (UUO) are potential sources of pro-inflammatory cytokines that exacerbate inflammation and fibrosis. The purpose of this study was to characterize intra-renal leukocytic infiltrate in the UUO model using HO-1 $-/-$ and wild-type (WT) mice to elucidate the immunoregulatory role of HO-1.

Methods Used: Kidneys were harvested 48 h following UUO and sham surgery in HO-1 $-/-$ and WT mice (C57BL/6, 6-14 weeks). Cell suspensions were prepared and stained with antibodies to identify the leukocytic subtypes by flow cytometry (Table 1).

TABLE 1. Summary of Results

Markers	HO-1 $+/+$		HO-1 $-/-$	
	UUO	Sham	UUO	Sham
Leukocytes: CD45+	3.1% $\pm$ 1.9 (n=6)	1.6% $\pm$ 1.7 (n=5)	4.9% $\pm$ 4.8 (n=3)	0.78% (n=1)
Inflammatory Macrophage: CD45+, MHC II+, Ly6C+ and Gr-1+	15.4% $\pm$ 8.8 (n=7)	2.5% $\pm$ 2.0 (n=5)	27.5% $\pm$ 13.1 (n=4)	1.8% $\pm$ 0.3 (n=2)
Inflammatory Macrophage: CD45+, MHC II+, CD11b+ and Gr-1+	19.9% (n=1)	2.5% $\pm$ 1.7 (n=2)	26.7% $\pm$ 12.8 (n=3)	2.1% (n=1)
Dendritic Cells: CD45+, MHC II+ and CD11c+	21.1% $\pm$ 4.6 (n=6)	52.1% $\pm$ 6.1 (n=7)	10.1% (n=1)	38.3% (n=1)
Dendritic Cells: CD45+, MHC II+, CD11c+ and Gr-1-	31.3% (n=1)	9.9% (n=1)	23.0% $\pm$ 2.2 (n=3)	20.8% (n=1)
Ambiguous Cells: CD45+, MHCII+, F4/80+ and CD11b+	46.7% $\pm$ 8.9 (n=7)	10.1% $\pm$ 5.8 (n=4)	56.5% $\pm$ 22.7 (n=4)	3.4% $\pm$ 0.8 (n=2)

Summary of Results: Leukocytic infiltration was increased in the UUO kidneys compared to contralateral and sham, this result was amplified in the HO-1 $-/-$ mice (Table 1). The proportion of inflammatory macrophages was increased in the UUO kidney in both WT and HO-1 $-/-$ mice, and this was exaggerated in HO-1 $-/-$ mice. DC's decreased in the UUO kidney in both WT and HO-1 $-/-$ mice compared to contralateral and sham, however adding Gr-1- as a negative DC marker increased this cell population in the UUO kidney. A subpopulation of F4/80+ and CD11b+ cells was increased in UUO kidneys both in WT and HO-1 $-/-$ mice.

Conclusions: The data suggest that absence of HO-1 expression increases pro-inflammatory macrophage infiltration following UUO and maybe responsible for increased renal fibrosis and inflammation observed in HO-1 $-/-$ mice.

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ATYPICAL HEMOLYTIC UREMIC SYNDROME (HUS) PRESENTING INITIALLY AS MALIGNANT HYPERTENSION

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Purpose of Study: A 10 month old previously healthy female infant presented with acute onset of facial & lower extremity edema. There was no evidence of diarrhea or change in urine output at presentation. Family history revealed male sibling who died at 4 months of age due an undetermined cause.

Methods Used: Physical examination revealed an alert afebrile infant with peripheral, facial and severe peri-orbital edema. Bilateral crackles were audible on the lung exam. Cardiac exam was unremarkable. The infant was warm, well perfused with good peripheral pulses and brisk capillary refill. She was found to have severe hypertension with blood pressure (BP) in the 200s systolic and 120s diastolic in all 4 extremities. Additional investigations revealed severe anemia with a hemoglobin and hematocrit of 6.0/16.2, respectively. Peripheral blood smear revealed schistocytes, consistent with microangiopathic anemia. Initial platelet count, serum creatinine, potassium and sodium bicarbonate were normal, but albumin was low at 2.5 mg/dl. Initial urinalysis demonstrated +3 proteinuria, +1 hemoglobin and 1-2 RBCs. 2D echo revealed presence of left ventricular hypertrophy (LVH). Imaging and hormonal studies excluded renovascular hypertension. Intravenous infusion of sodium nitroprusside was started in an effort to decrease the BP. Lasix was initiated in an attempt to minimize edema. Packed RBCs were given to correct anemia. Hospital course was characterized by progressive azotemia, oliguria and thrombocytopenia. Renal biopsy revealed presence of thrombotic microangiopathy. A clinical diagnosis of diarrhea-negative (atypical) HUS was established and targeted investigations were commenced. Daily plasmapheresis was promptly initiated. Progressive azotemia required later initiation of CVVHD. Despite intensive therapy, patient died from fatal cardiac arrhythmia.

Summary of Results: Molecular analysis revealed absence of mutations in complement factor I (CFI), complement factor B (CFB), complement factor H-related 5 (CFHR5), membrane cofactor protein (MCP), complement C3 and presence of 158G>A transition in complement factor H (CFH) of unknown significance.

Conclusions: This case illustrates importance of high index of suspicion for this rare disease where 25% of children are likely to die during the acute phase.

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CONGENITAL URIC ACID NEPHROLITHIASIS: A CASE REPORT

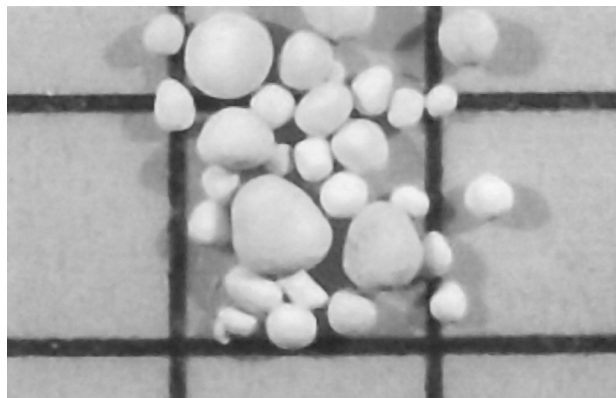
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Case Report: Congenital nephrolithiasis is rare, with only very few cases in literature. However, there are no reported cases of congenital nephrolithiasis with the infant passing uric acid stones on 3rd day of life.

We report the case of a term male infant who presented with gross hematuria on 1st day of life. UA revealed pH of 9 and large blood (>100 RBCs). Chemistry, CBC and Coag panel were normal. Random urine electrolytes, including Ca/Cr ratio were also normal. KUB was unremarkable, however, renal ultrasound revealed hyperechoic foci and posterior shadowing consistent with renal calculi bilaterally. NaHCO3 drip and IV hydration was initiated. On day 3 of life, infant started passing 'gravel' consisting of small white round stones. Stones were sent for chemical analysis. Serum uric acid was low at 1.6 (3.5-7.2). But random urine uric acid excretion (adjusted for GFR) was high at 0.62 (<0.56). 24 hr urine citrate level was low and uric acid was high at 20 mg/kg/day (<19.6 mg/kg/day). Renal scan revealed normal bilateral renal function. Metabolic work up was also normal. Stone excretion and hematuria stopped on day 6 of life. Repeat UA was normal. NaHCO3 was changed to oral bicitra. Chemical analysis of stone returned as 100% sodium acid urate. Bicitra was continued for 3 months. Renal ultrasound repeated at 3

months of age did not show any evidence of stones and uric acid excretion was also normal.

Uric acid stones can be associated with rare genetic and metabolic disorders. This case highlights the presentation of hematuria with uric acid stone formation in a neonate and should heighten the clinician's differential when faced with gross hematuria.



Uric acid stones passed by infant.

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I CANNOT SEE MY PEE: JUVENILE NEPHRONOPHTHISIS

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Case Report: A 13 years old Caucasian female who was referred to our center on account of anemia, 5-months history of fatigue, malaise, dizziness, loss of appetite and 20 pounds weight loss. Past medical history was significant for Leber's congenital amaurosis (LCA) and congenital blindness. Review of system revealed no hypertension, polyuria nor polydipsia. Family history was negative for consanguinity and positive for renal stone formation in dad and congenital single kidney in maternal aunt. Physical examination was essentially normal except for tachycardia, weight and height of great than 97% for age. Admission labs show sodium 128, potassium 3.1, BUN 63 and creatinine 8.3. Hemoglobin and hematocrit were 7.6 and 21.4 respectively. Urine specific gravity was 1.012, with trace protein. Renal ultrasound showed bilaterally small kidneys, poor cortical medullary differentiation, increased cortical echogenicity, and small cystic foci within the cortex and medulla. A diagnosis of juvenile Nephronophthisis with End State Renal Failure (ESRF) was made. The patient received series of peritoneal dialysis; both clinical and laboratory status improved and was discharged home. Patient is currently doing well and she is being prepared for renal transplant while on peritoneal dialysis. Juvenile Nephronophthisis is characterized by bilateral small cortico-medullary cysts in normal or reduced sized kidneys and tubule-interstitial sclerosis leading to ESRD. Nephronophthisis has an autosomal recessive inheritance pattern and 7 distinct genes (designated as NPHP1, NPHP4, NPHP5, NPHP6, NPHP7, NPHP8, and NPHP9). The median age of onset of ESRD is 13 years. Although this case has a classical presentation but it also highlighted the need for physician to evaluate for associated conditions in a patient who presented with a congenital abnormality. There is also the need for interdisciplinary health management approach in patients with congenital anomaly. The patient and her parents did not anticipate this renal complication. Failure to recognize nephronophthisis in a child with polyuria, anemia, growth retardation, and normal kidney function is a major medicolegal pitfall.

Cardiovascular II

8:00 AM

Saturday, February 27, 2010

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CHRONIC ATRIAL FIBRILLATION AND PROLONGED QT_c INTERVAL IN A PATIENT WITH THE GITELMAN SYNDROME

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Case Report: Purpose. Electrolyte disturbances will contribute to the appearance of cardiac arrhythmias. Atrial fibrillation (AF) and prolonged QT_c (≥ 460 ms) can have diverse etiologic origins; however, two of the more common and often overlooked factors are hypokalemia and hypomagnesemia. Gitelman, Bartter, Liddle, and Conn syndromes are uncommon causes of hypokalemia, but they should be kept in mind as causes of unexplained hypokalemia with metabolic alkalosis.

Case Report: A 53-year-old Caucasian man presented in May, 2009 with AF and prolonged QT_c (500ms). He denied nausea, vomiting, diarrhea, muscle cramps, alcohol abuse or smoking. He also had a family history of chronic AF and four siblings, a mother, and maternal grandmother with an unknown "electrolyte disorder." The patient was not taking diuretics or any drugs known to prolong the QT_c interval at the time of presentation or at any time during his hospital course. Initial vital signs and laboratory values revealed he had an unexplained normotensive, hypomagnesemic (1.7 mg/dL), hypokalemic (3.5 mmol/L) metabolic alkalosis (HCO₃ 29 mmol/L; pH 7.50). All other laboratory values, including thyroid stimulating hormone, renin, and aldosterone were within normal limits. Subsequent urine studies revealed he was "wasting" potassium (defined as fractional excretion $>15\%$ and transtubular potassium gradient >3.0) and magnesium (defined as fractional excretion $>4\%$). Furthermore, he exhibited hypocalciuria (defined as urine Ca/urine Cr ratio <0.10), which distinguished his potassium/magnesium-wasting nephropathy as the Gitelman not Bartter syndrome. Spironolactone and magnesium replacement were effective in correcting his hypokalemia and hypomagnesemia.

Conclusion: The Gitelman syndrome, as well as the syndromes of Bartter, Conn, Liddle and Cushing are unusual yet important causes of electrolyte imbalance. Each may not only be associated with ventricular but also atrial arrhythmias, such as AF. In the Gitelman syndrome, spironolactone is effective in correcting electrolyte abnormalities. We believe the correction of our patient's underlying metabolic disturbances will lead to fewer symptomatic episodes of AF and a reduced risk of adverse cardiac events related to a prolonged QT_c interval.

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LEFT VENTRICULAR DYSSYNCHRONY BY PHASE ANALYSIS AS A PREDICTOR OF MORTALITY IN END-STAGE RENAL DISEASE

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Purpose of Study: Cardiovascular disease is the leading cause of mortality in patients with end-stage renal disease (ESRD). We have shown that left ventricular (LV) ejection fraction (EF) is a major determinant of survival in ESRD. The prognostic importance of LV dyssynchrony has not been well studied.

Methods Used: We measured indices of LV mechanical dyssynchrony by automated analysis of gated SPECT myocardial perfusion imaging in ESRD patients evaluated for transplantation at our institution (2000–2004) who had coronary angiography. All-cause mortality data was prospectively collected and verified against the social security death index database.

Summary of Results: The study population consisted of 144 ESRD patients (53±9y, 35% female, 63% diabetes mellitus, LVEF 48±12%) who were followed up for 41±28 months during which 55 (38%) died prior to renal transplantation. The median phase bandwidth (BW) was 62 (range 22–264) and standard deviation (SD) was 23 (range 4–71). Patients with a BW above the median had worse survival (log-rank P=0.017) and there was a trend towards worse survival in those with a SD above the median (log-rank P=0.096). 2-year mortality was higher in those with BW $\geq$ 62 in the entire

	BW<62	BW $\geq$ 62	p-value
Entire cohort	4/68 (6%)	17/76(22%)	0.008
LVEF $\geq$ 50%	2/48 (4%)	4/17 (24%)	0.02
LVEF<50%	2/15 (13%)	11/57(19%)	0.5
No CAD	1/22 (5%)	2/16 (13%)	0.6
CAD	3/44 (7%)	15/60(25%)	0.018
No LVH	3/36 (8%)	7/41(17%)	0.3
LVH	1/32 (3%)	10/3(29%)	0.007

CAD = coronary artery disease, LVH = left ventricular hypertrophy.

cohort, and in the subset of patients with normal LVEF, coronary artery disease by angiography, and LV hypertrophy by electrocardiography (Table). **Conclusions:** LV mechanical dyssynchrony by phase analysis is a predictor of mortality in patients with ESRD and may have a role in risk-stratifying patients with normal LVEF.

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ROLE OF ADIPONECTIN IN AUTOPHAGY AND PATHOLOGICAL CARDIAC HYPERTROPHY

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Purpose of Study: Pathological cardiac remodeling is a leading cause of heart failure, a syndrome of epidemic proportions today. Mechanisms whereby pathological cardiac hypertrophy transforms to systolic dysfunction and heart failure are unknown, but autophagy and adiponectin have been implicated. Adiponectin has been associated with improved outcomes after myocardial infarction, and some evidence suggests that adiponectin promotes autophagy in cultured cardiomyocytes.

Methods Used: To explore the relationship between adiponectin, cardiomyocyte hypertrophy, and autophagy, we tested the effects of adiponectin on the heart in vitro and in vivo. First, neonatal rat cardiomyocytes (NRCMs) were exposed to adiponectin, phenylephrine (PE), PE combined with adiponectin, or control medium, and we tested for markers of autophagic and fetal gene program activation. Next, we studied wild-type and adiponectin-over-expressing transgenic mice. Here, we performed transverse aortic constriction (TAC) to induce cardiac hypertrophy and food deprivation (36h) to induce autophagy. Animals were evaluated for clinical and morphological criteria of pathological cardiac remodeling, and autophagic markers were quantified.

Summary of Results: In vitro, NRCMs treated with adiponectin expressed higher levels of the hypertrophic markers ANF and BNP, compared to control. Adiponectin-treated cells manifested lower levels of autophagy compared to control, as measured by the abundance of the autophagosome marker LC3-II. Adiponectin transgenic mice displayed increased heart mass (heart weight/body weight, heart weight/tibial length ratios) compared to their wild-type counterparts under basal conditions, or following TAC or sham operations. Heart tissue from transgenic mice also displayed higher levels of ANF and BNP compared to control. TAC elicited autophagy in both wild-type and adiponectin transgenics, but the amount of autophagic activation was significantly lower in transgenic animals.

Conclusions: Adiponectin promotes hypertrophy and inhibits autophagy in animal models of pathological cardiac remodeling. Taken together, these studies provide insight into important links between cardiovascular disease and metabolic syndrome.

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TRANSCRIPTIONAL REGULATION AND EXPRESSION OF GUANYLYL CYCLASE/NATRIURETIC PEPTIDE RECEPTOR-A GENE BY TGF- β 1 IN MOUSE MESANGIAL AND VASCULAR SMOOTH MUSCLE CELLS

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Purpose of Study: The binding of atrial and brain natriuretic peptides (ANP and BNP) to guanylyl cyclase-A/natriuretic peptide receptor-A (GC-A/NPR-A) produces second messenger cGMP, which plays a critical role in various intracellular signaling pathways including: hypertension, cardiovascular events, and cancer. Recent studies have revealed that the cis-response elements in the 5' flanking region of Npr1 gene (coding for GC-A/NPRA) promoter play a key role in regulating the expression and function of the receptor protein. δ EF1, an E-2 box repressor has been predicted to have binding sites in the 5' flanking region of the Npr1 gene promoter. Transforming growth factor- β 1 (TGF- β 1) is a cytokine, which inhibits Npr1 gene expression while δ EF1 has been known to mediate TGF- β 1 signaling. The objective of this study was to determine the repressive effect of TGF- β 1 on transcriptional regulation of murine Npr1 gene promoter in mouse mesangial cells (MMCs) and rat thoracic aortic vascular smooth muscle cells (RTASMCs).

Methods Used: MMCs were cultured in Dulbeccos modified Eagle's medium (DMEM) containing 10% fetal bovine serum (FBS) and ITS (insulin, transferrin, and selenium). RTASMCs were cultured in DMEM containing

10% FBS. All cultures were maintained at 37° C in an atmosphere of 50% CO₂ and 90% O₂. Cells were transiently transfected using Lipofectamine-2000 and promoter activity was measured by utilizing dual luciferase assay.

Summary of Results: Co-transfection of δ EF1 expression plasmid with the Npr1 gene promoter-luciferase constructs showed 70–75% reduction in the luciferase activity in MMCs and RTASMCs. Also, Npr1 gene promoter-luciferase constructs embodying δ EF1 sites showed reduction in luciferase activity after treatment with TGF- β 1 in a time- and dose- dependent manner. **Conclusions:** The findings of this study are vital in understanding TGF- β 1 signaling and its effect on Npr1 gene transcription and expression which plays a critical role in cardiovascular regulation.

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ELEVATIONS OF PLASMA BRAIN NATRIURETIC PEPTIDE AND VITAMIN B₁₂ IN STRATIFYING CENTRAL AND SYSTEMIC CONGESTION IN HEART FAILURE

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Purpose of Study: Abnormal elevations in plasma brain natriuretic peptide (BNP) are used as a biomarker of central congestion along with atrial and/or ventricular distention and to assess for decompensated heart failure. However, BNP fails to gauge for systemic venous congestion. Contrariwise, abnormal elevations in serum vitamin B₁₂ (or cobalamin), released from congested hepatic sinusoids are a biomarker of systemic congestion (Zafarullah H, et al. *Am J Med Sci* 2008;336:383–88). In this study we addressed the use of both biomarkers in patients hospitalized with heart failure, with or without systemic congestion, or no clinical evidence of heart failure.

Methods Used: Medical records were retrospectively examined on 55 patients, hospitalized at an urban medical center over a 3-month period and in whom admission values for plasma BNP and B₁₂ were available. They included: 13 patients (12M; 49 $\pm$ 2 yrs), who presented with findings of decompensated, biventricular failure (DecompHF); 17 patients (9M; 57 $\pm$ 4 yrs) with signs of acute left heart failure (LHF); 10 patients (5M; 49 $\pm$ 4 yrs) with heart disease, but no clinical evidence of heart failure (HDNHF); and 15 patients (6M; 53 $\pm$ 6 yrs) without cardiovascular disease (NCVD), who served as controls.

Summary of Results: Normal BNP <100 pg/mL; normal B₁₂ <600 pg/mL. Mean $\pm$ SEM values are shown below. Abnormal elevations in plasma BNP were found in all patients with DecompHF and acute LHF, 50% of those with HDNHF, and only one with NCVD. Elevations in BNP were marked in patients with DecompHF and acute LHF compared to HDNHF. Serum B₁₂ was only elevated in patients with DecompHF.

Conclusions: Marked elevations in BNP distinguish central congestion from the elevated peptide levels seen with atrial and ventricular distention associated with HDNHF. Elevations in serum B₁₂ distinguish DecompHF with hepatic congestion from acute LHF. By combining B₁₂ with BNP monitoring in patients with heart failure the presence or absence of systemic and central congestion can be stratified.

	DecompHF	Acute LHF	HDNHF	NCVD
BNP	1300 $\pm$ 219	732 $\pm$ 108	237 $\pm$ 87	51 $\pm$ 20
B ₁₂	895 $\pm$ 79	458 $\pm$ 32	323 $\pm$ 24	360 $\pm$ 31

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ANGIOTENSIN II INFUSION DISRUPTS ADP/ATP BALANCE AND AMPK ACTIVATION, CONTRIBUTING TO WASTING IN SKELETAL MUSCLE OF FVB MICE

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Purpose of Study: Congestive heart failure is accompanied by elevated circulating angiotensin II (AngII) and skeletal muscle wasting, which correlates strongly to poor prognosis. AngII induced muscle wasting is due primarily to accelerated protein degradation and suppression of protein synthesis. This study aims to determine whether AngII alters cellular energy stores in skeletal muscle, and to characterize mechanisms involved in order to ascertain whether energy depletion plays a role in skeletal muscle wasting.

Methods Used: Mitochondria were quantified via real-time PCR and MitoTracker® staining. Mitochondrial activity was assessed with MitoSox™ staining and Cytochrome C Oxidase (COX) Activity Assay. Energy availability was assayed via an ADP/ATP Ratio Assay Kit. AMPK activation was measured with SDS-PAGE and Western Blotting.

Summary of Results: Infusion of AngII via osmotic minipump in FVB mice resulted in a marked 55% reduction of mitochondrial content after 4 days in tibialis anterior (TA) muscle, with a corresponding 26% reduction in mitochondrial superoxide, and an apparent compensatory 86% increase in COX activity. These effects were independent of food intake (FI). No changes in mitochondrial content were observed in quadriceps (Quad) or gastrocnemius (Gas) muscles; however, we found a FI independent 45–47% reduction in COX activity in Gas and Quad in response to AngII. All muscles displayed a 76–85% reduction in ATP and a 1.8 to 2.6 fold increase in ADP/ATP ratio with AngII infusion. In response to lowered cellular energy availability, AMPK activation was increased 40% in TA. Interestingly, AngII actually reduced AMPK phosphorylation in Quad independently of FI, with a similar trend in Gas.

Conclusions: AngII reduces skeletal muscle mitochondrial content or activity, ultimately leading to a reduction in energy availability. It is interesting that TA tends to be more resistant to AngII induced wasting than Gas or Quad in this model. Our data suggest that AMPK activation is compensating for reduced energy availability in TA by curbing energy demanding cellular processes and inducing mitochondrial biosynthesis. The failure of Quad and Gas to react in a similar manner to the energy imbalance may partially explain why these muscles are more sensitive to AngII induced wasting than is TA.

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UNCOUPLING THE COUPLED CALCIUM AND ZINC DYSHOMEOSTASIS IN CARDIAC MYOCYTES AMELIORATES CARDIAC OXIDATIVE STRESS IN ALDOSTERONISM

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Purpose of Study: Parathyroid hormone-mediated intracellular $[Ca^{2+}]_i$ overloading in cardiomyocytes and mitochondria is a fundamental pathogenic event associated with the secondary hyperparathyroidism (SHPT) that accompanies chronic aldosterone/salt treatment (ALDOST). It accounts for an induction of oxidative stress that leads to necrotic cell death and consequent myocardial scarring. This prooxidant response to Ca^{2+} overloading in cardiac myocytes and mitochondria is intrinsically coupled to simultaneous increased Zn^{2+} entry serving as an antioxidant. Herein, we investigated whether Ca^{2+} and Zn^{2+} dyshomeostasis and prooxidant:antioxidant dysequilibrium seen at 4 wks, the pathologic stage of ALDOST, could be uncoupled in favor of antioxidants.

Methods Used: Eight-wk-old uninephrectomized rats received 4 wk ALDOST alone or with cotreatment: a $ZnSO_4$ supplement; pyrrolidine dithiocarbamate (PDTC), a Zn^{2+} ionophore; or $ZnSO_4$ in combination with amlodipine ($ZnSO_4$ +Amlod), a Ca^{2+} channel blocker. Unoperated/untreated age-/sex-matched animals served as controls. We monitored and compared responses in cardiomyocyte free $[Ca^{2+}]_i$ and $[Zn^{2+}]_i$, together with biomarkers of oxidative stress, in cardiac myocytes and mitochondria.

Summary of Results: At wk 4 ALDOST and compared to controls, we found: i) an elevation in $[Ca^{2+}]_i$ coupled with $[Zn^{2+}]_i$; and ii) increased mitochondrial H_2O_2 production, and increased mitochondrial and cardiac 8-isoprostane levels. Cotreatment with the $ZnSO_4$ supplement alone, PDTC, or $ZnSO_4$ +Amlod augmented the rise in cardiomyocyte $[Zn^{2+}]_i$, beyond that seen with ALDOST alone, while attenuating the rise in $[Ca^{2+}]_i$ which together served to reduce oxidative stress as gauged by a fall in mitochondrial H_2O_2 production and cardiac 8-isoprostane.

Conclusions: Thus, a coupled dyshomeostasis of intracellular Ca^{2+} and Zn^{2+} was demonstrated in cardiac myocytes during 4 wks ALDOST. This intrinsically coupled Ca^{2+} and Zn^{2+} dyshomeostasis could be uncoupled in favor of antioxidant defenses by selectively increasing cytosolic free $[Zn^{2+}]_i$ and/or reducing $[Ca^{2+}]_i$ using cotreatment with $ZnSO_4$ or PDTC alone or $ZnSO_4$ +Amlod in combination.

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UPREGULATION OF SCA-1 IN SATELLITE CELLS DURING DIAPHRAGMATIC SKELETAL MUSCLE REGENERATION: POTENTIAL NOVEL MECHANISM OF SKELETAL MUSCLE REGENERATION

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Purpose of Study: Stem cell antigen-1 (Sca-1) is an 18kDa glycosyl phosphatidylinositol-anchored cell surface protein of the Ly-6 family that is

involved in cell activation, proliferation and differentiation. Regeneration of skeletal muscle is a multifactorial process which includes proliferation and differentiation of satellite cells into new muscle fibers. Mechanisms of skeletal muscle regeneration, however, are poorly understood. We previously reported that angiotensin II (Ang II) is implicated in the induction of skeletal muscle atrophy that is characteristic of advanced heart failure. This study was designed to investigate the effects of Ang II on diaphragmatic skeletal muscle and determine mechanism(s) of skeletal muscle regeneration.

Methods Used: FVB mice were infused with $1\mu g/Kg/min$ Ang II or sham-infused for one week.

Summary of Results: Immunostaining for embryonic myosin heavy chain revealed multiple areas of regenerating muscle fibers and Sca-1 expression was markedly upregulated in the satellite cells of these injured areas. To quantitate Sca-1 expression we isolated diaphragmatic muscle stem cells using collagenase followed by pronase and finally analyzed by FACS. Our results showed that Ang II infusion significantly increased the levels of Sca-1 positive cells in the injured diaphragmatic muscle preparation (Ang II, $43.97 \pm 2.03\%$ vs Sham, $37.77 \pm 1.71\%$ $p < 0.05$) suggesting that satellite cell Sca-1 expression may play a role in the ability of these cells to acquire an embryonic stem cell character and to proliferate and differentiate into new skeletal muscles. To verify this hypothesis, we analyzed proliferation and myogenesis indices in the injured diaphragmatic skeletal muscle. Both proliferation markers PCNA and Ki67 were upregulated as detected by Western blot for PCNA and immunostaining for Ki67. The myogenic factor, M-cadherin was also increased in the injured muscle.

Conclusions: In conclusion, our results demonstrate that Ang II induced injury of diaphragmatic skeletal muscle is accompanied by increased proliferation and myogenesis that is potentially mediated, at least in part, by increased activity of Sca-1 in muscle satellite cells.

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QTc INTERVAL RESPONSIVENESS TO THE APPEARANCE OR FOLLOWING THE CORRECTION OF HYPOKALEMIA

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Purpose of Study: A lengthening of the duration of repolarization, as reflected in a prolongation of the QTc interval found on the routine electrocardiogram, enhances the vulnerability of the heart to atrial and ventricular arrhythmias. QTc prolongation also suggests the presence of an electrolyte abnormality, such as hypokalemia, while a normalization of the QTc interval may be in keeping with the resolution of hypokalemia. This study was undertaken to address the utility of serial QTc interval monitoring in addressing the appearance or correction of hypokalemia.

Methods Used: This retrospective study was conducted in 24 patients followed at an urban medical center and in whom serial routine electrocardiograms had been obtained during August, 2009, together with serum electrolytes. We addressed the response in the QTc interval to: a) the appearance of hypokalemia (≤ 3.6 mEq/L) which was found in 13 previously normokalemic patients (4 M; 54 ± 5 yrs); and b) correction of serum K^+ rising to ≥ 3.9 mEq/L in 11 previously hypokalemic patients (6 M; 56 ± 3 yrs).

Summary of Results: In normokalemic patients (4.10 ± 0.1 mEq/L) who became hypokalemic (3.37 ± 0.05 mEq/L), we found the QTc interval to increase to 477 ± 8 ms from a baseline of 441 ± 9 ms/L. Four of these 13 patients developed atrial fibrillation in association with hypokalemia. In 11 patients who had been hypokalemic (3.42 ± 0.04 mEq/L) with prolonged QTc (492 ± 37 ms), the QTc interval was normalized to 444 ± 10 ms with the correction of serum K^+ (4.21 ± 0.11 mEq/L).

Conclusions: Serial monitoring of QTc and QTc interval prolongation in particular, an indirect measure of myocardial repolarization and the intracellular to extracellular K^+ gradient. It can provide complementary information in addressing the importance of disturbances in extracellular K^+ , as reflected in serum K^+ levels, and the heart's vulnerability to arrhythmias. Monitoring QTc responsiveness and normalization to the resolution of hypokalemia can prove useful in gauging the adequacy of K^+ replacement.

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IMPAIRED CORONARY VASCULAR REACTIVITY IN CARDIAC SYNDROME X MEASURED NON-INVASIVELY BY 3T MRI

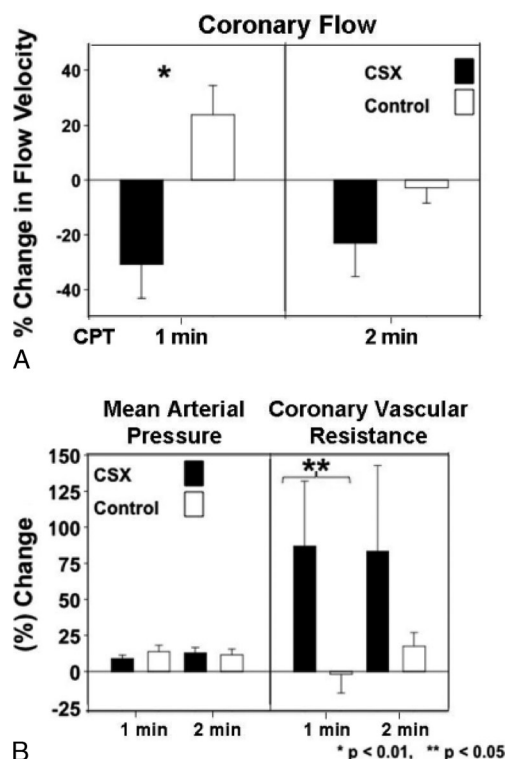
T. Yee, E. Holper, M. Kotys, R. Peshock, A. Chang *UT Southwestern, Dallas, TX.*

Purpose of Study: Cardiac syndrome X (CSX) describes women with chest pain, abnormal stress tests but no significant coronary stenoses by angiography. Impaired coronary vascular reactivity (CVR) predicts cardiovascular events in CSX. Non-invasive detection of impaired CVR could facilitate early diagnosis and risk stratification in CSX. We previously demonstrated significant increases in coronary flow (CF) in healthy women using 3T magnetic resonance imaging (MRI) and the cold pressor test (CPT). We sought to determine if women with CSX had impaired CVR compared to matched controls using MRI.

Methods Used: We recruited 7 women with CSX and 8 controls matched for cardiac risk factors. Using 3T MRI, baseline CF was obtained using a spiral, velocity-encoded, cine sequence perpendicular to the right coronary artery (spatial resolution = $0.8 \times 0.8 \times 7$ mm³, temporal resolution = 69 ms). Images were acquired during 2 min of CPT. Peak CF was measured during diastole.

Summary of Results: There was no significant difference in age, body mass index, prevalence of diabetes or baseline blood pressures between groups. There was no significant difference in % increase in rate pressure product to CPT (CSX $30.9\% \pm 14$, controls $40.9\% \pm 28$; $p = 0.67$). During CPT, CSX women demonstrated a significant early decrease in CF (Fig. 1A), associated with increases in coronary vascular resistance not seen in controls (Fig. 1B).

Conclusions: Impairment in CVR is detectable non-invasively by 3T MRI with CPT in CSX women compared to matched controls.



Allergy, Immunology, and Rheumatology II Concurrent Session

1:00 PM

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25-OH-VITAMIN D LEVELS DIFFER IN PATIENTS WITH SJOGREN'S SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Purpose of Study: We tested the 25-OH-Vitamin D (Vitamin D) levels in patients with Sjogren's syndrome as well as in symptomatic patients (dry eyes and dry mouth) who did not meet the criteria for Sjogren's syndrome. As Vitamin D has been shown to be low in patients with various autoimmune diseases, we compared our data to data on Vitamin D levels in SLE patients.

Methods Used: 144 consecutive patients seen in the Sjogren's clinic in Oklahoma City were classified as having Primary Sjogren's (pSS), Sjogren's secondary to another autoimmune disease (sSS), or not meeting criteria for a diagnosis (DNMC). A pSS diagnosis was considered positive when 4 of 6 of the following criteria were met: dry eyes, dry mouth, low unstimulated salivary flow, positive Schirmer test, positive lip biopsy and positive anti-Ro antibodies. A positive lip biopsy was determined by focal scores on consensus from two dental pathologists. Ro 60 status was determined by ELISA, immuno-diffusion, or radioimmunoassay. There were 64 pSS patients, 59 DNMC, and 21 sSS. 25-OH-Vitamin D levels were measured from patients' sera using a commercial ELISA kit (IDS Ltd). Patients' Vitamin D status was defined as "sufficient" (>80 nmol/L), "insufficient" (37.5-80 nmol/L), or "deficient" (<37.5 nmol/L).

Summary of Results: The average Vitamin D level for pSS was 108 nmol/L, ± 36 (43 ng/mL, ± 14), with 81% of patients being considered "sufficient." For DNMC, the average was 95 nmol/L, ± 37 (37 ng/mL, ± 14), with 61% considered "sufficient". For sSS, the average was 91 nmol/L, ± 37 (36 ng/mL, ± 14), with 62% "sufficient." A t-test comparing the pSS group and the DNMC group produced a p-value of 0.051.

Conclusions: The mean 25-OH-Vitamin D level amongst Sjogren's patients had slightly higher Vitamin D levels than the DNMC group, however, there was statistically no difference between the two groups. This result is in direct contrast to many autoimmune diseases. Specifically, these results highlight a difference in our patient population between Sjogren's syndrome and SLE, where SLE has been consistently shown to have low Vitamin D levels.

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GENES AND CYTOKINE EXPRESSION PROFILE IN IDIOPATHIC JUVENILE OSTEOPOROSIS

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Purpose of Study: To study the gene expression and regulatory biomarkers of bone turnover in a patient with osteoporotic vertebral fracture (T12) while on Bisphosphonates.

Methods Used: Peripheral blood mononuclear cells were isolated from the Patient, her Parents and 5 young controls. Starting with total RNA, Osteogenesis and Wnt Signaling Pathway RT Profiler PCR for 84 genes was used. TNF- α , DKK-1, RANK, WIF, OPG, sIL-1 R, sTNF RI/II, sIL-6 R, IL-15, IL-7, IL-12, IL-17, IL-23, IFN- $\alpha/\beta/\gamma$, EGF, VEGF, Adiponectin, Leptin were assessed by ELISA. DEXA scan was done (Subject 2005 T score L-spine -3.3/ Femur -2.5; in 2009 T score L-spine -2.3/ Femur -2.1). Causes of secondary osteoporosis were ruled out. Normal limits (mean ± 2 S.D.) were computed for all biomarkers.

Summary of Results: PCR assays from the Patient, Father and Mother showed: In Osteogenesis Pathway, genes: 6/84, 32/84, 37/84 were up regulated and 22/84, 16/84, 11/84 were down regulated. In Wnt signaling Pathway 5/84, 17/84, 20/84 were up regulated and 19/84, 19/84, 16/84 were down regulated as compared to healthy controls. In the Patient, SMAD2(-2.4), TGF β 2 and 3(-3.10, -2.69), TGF β RI(-2.71), IGF-1(-5.57), FZD1(-2.61), FZD5(-4.88), SFRP4(-30.16), CSNK1G1(-9.74), KREMEN1(15.11), LRP6(-2.33), NKD1(-3.68) and WIF1(2.61). Main variations in gene expression in the father were FZD3 (-2.23), FZD4(-2.18), FZD5(-5.63), FZD7(-2.38), WNT4(-6.57), WNT16(-3.87), DKK1(2.55), FRZB(3.18), SFRP4(-5.43), TCF7L1(-4.71), WISP (-6.80), TCF7L1 (-4.71), CSNK1G1(-6.62), BTRC(-2.65), KREMEN1(-6.34), CSF3 (3.22), BMP1(-2.67), BMP6(-3.3), TGF β RI(-3.43). Mother gene expression showed FZD6 (-6.21), WNT2B (-2.45), WNT4(-5.30), DKK1(8.12), SFRP1(8.12), WISP1(8.12), SOX17 (8.12), TLE(-17.52), WIF1(8.12), BCL9(-26.30), KREMEN1(47.25), IGF1R(-4.96), TGF β 3(-42.81), TGF β RI(-8.57), SMAD2 (-3.29), TWIST1 (6.06). Serologic biomarkers in subject compared to the controls: OPG, IFN- γ were up regulated and sTNF RII down regulated.

Conclusions: Patient showed down regulation of receptors and co receptors of the Wnt/ β -catenin pathway; and upregulation of inhibitory factors (WIF 1, KREMEN 1) of the Wnt cascade. Patient's OPG and IFN- γ levels were increased which favors osteoblast function and differentiation most likely due

to the anti inflammatory effect of the bisphosphonates supported by the serial DEXA scores.

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FEWER MALE SIBLINGS AND INCREASED MALE FETAL LOSS IN A COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS FAMILIES

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Purpose of Study: A sex bias has been found absent in sibships of non-female predominant diseases like diabetes. We undertook this study to enhance our understanding of sex ratios in live sibships and lost fetuses in a large cohort of Systemic lupus erythematosus (SLE).

Methods Used: Families were collected through the Lupus Family Registry and Repository. All patients met atleast 4 of the 1982 ACR classification criteria for SLE. All families had atleast one member with SLE. Collective sibling gender data were obtained for the SLE cohort studied. Spontaneous miscarriage and abortion information was assessed, when self-reported, on a standard questionnaire filled by the patient. Male to female sex ratios were calculated.

Summary of Results: Collectively, 282 SLE affected male patients had 314 male siblings and 415 female siblings. The 2296 SLE affected female patients had 3113 male siblings and 3772 female siblings. Thus the ratio of male to female siblings = $(314+3113) / (3772+415) = 0.82$. SLE affected females reported 36 events of male fetal loss and 20 events of female fetal loss. Thus, ratio of male to female fetal loss was found to be 1.8:1.

Conclusions: There is a trival explanation for too few male siblings in this cohort. Sibships with lots of girls are more likely to have SLE because of the excess girls with SLE and, therefore are more likely to be included in the study. So, to correct for the ascertainment bias, we left out the SLE patients. Even when doing this, the male/female ratio is 0.8 and live births and fetal loss is nearly twice more common in males. The most parsimonious and perhaps the only explanation is a gene on X where a mutation or allele is lethal for males in utero and gives girls risk for SLE as we have discussed. This means this gene should be on the maternal X chromosome of patients in families where the sibship containing the SLE patient has excess girls and/or there are reports of male fetal loss.

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DEVELOPMENTAL RESTRICTIONS ON MOUSE IMMUNOGLOBULIN DH AND JH USAGE PARALLEL RESTRICTIONS OBSERVED IN HUMAN FETAL LIFE

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Purpose of Study: The ability to generate antibodies to specific antigens develops in a controlled, programmed fashion during fetal life. This process occurs in parallel with the controlled, programmed development of antibody repertoire diversity. In human, control of repertoire diversity is associated with developmental restrictions in the pattern of DH and JH usage. These gene segments play a key role in regulating the diversity of the third complementarity determining region of the H chain, or CDR-H3, which lies at the center of the antigen binding site and plays an often determinative role in antigen binding specificity and affinity. Previous studies in mouse have identified development restrictions in the use of VH gene segments and in the ability to introduce non-germline encoded N nucleotides into CDR-H3. However, the developmental pattern of DH and JH usage remains unclear.

Methods Used: To test whether DH and JH usage is developmentally regulated, we used surface expression of CD43, BP-1, CD19, IgM and IgD to sort B lineage cells from BALB/c 18-day fetal liver, neonatal liver, and adult bone marrow. We then used RT-PCR to amplify VH7183-containing VDJCμ transcripts and subsequently compared patterns of VDJ usage in the perinatal period to those observed in young adults.

Summary of Results: We confirmed the previously reported preference for use of the VH81X gene segment fetal pro-B cells. However, contrary to previous studies using unsorted B lineage cells, we identified a shift from JH-proximal DHQ52 & DSP and DH-proximal JH2 in the perinatal period to JH-distal DHDFL16.1 and DH-distal JH3 & JH4 in the adult.

Conclusions: These results indicate that the regulation of the ontogeny of the antibody repertoire in mouse shares more similarities with human than previously appreciated. This work was supported, in part, by NIH AI07051 and AI48115.

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BOTH THE B1 AND B2 PERITONEAL CAVITY ANTIBODY CDR-H3 REPERTOIRES APPEAR TO BE INFLUENCED BY THE SAME SELECTIVE PRESSURES

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Purpose of Study: Natural antibodies (NABs) are defined as immunoglobulins that circulate in normal individuals in the absence of exogenous antigenic stimulation. NABs have been shown to provide one of the first lines of defense against both bacterial and viral pathogens. Although the key role played by the natural antibody repertoire in host defense is increasingly appreciated, major questions regarding the forces that shape its composition and thus control its binding characteristics and function remain. The B1a and B1b cells of the peritoneal cavity (PEC) are viewed as a major source of NABs. CDR-H3, which is created by VDJ joining and N nucleotide addition, lies at the center of the antigen binding site and thus plays a key role in antibody specificity and affinity. B1a CDR-H3 intervals demonstrate a paucity of N nucleotides, a feature that they share with antibodies created during the perinatal period.

Methods Used: To gain insight into the forces shaping the CDR-H3 repertoire in PEC B cells, we compared the sequences of VH7183DJCμ transcripts from sorted B1a, B1b and B2 cell subsets to those expressed by mature recirculating B cells (Hardy fraction F) in neonatal liver (NL F) and bone marrow (BM F) from BALB/c mice.

Summary of Results: VH and amino acids usage in B1a CDR-H3s lacking N regions (N-) proved nearly identical to that of mature, recirculating B cells from neonatal liver, whereas B1a sequences containing N regions (N+) were more similar to BM F, supporting the view that B1a cells expressing CDR-H3s with N nucleotides are derived from post-natal bone marrow. Unexpectedly, we found that the B2 compartment also demonstrated evidence of restriction in CDR-H3 sequence. While the VH repertoire in N+ B2 sequences shared extensive similarity with BM F, the CDR-H3 repertoire shared greater similarity with the B1a and B1b N+ repertoire than with BM F.

Conclusions: These findings suggest that the CDR-H3 repertoire expressed by the B2 compartment, which is presumed to be the source of adaptive immunity, appears to be shaped by the same antigen-receptor based selective pressures that influence the B1 CDR-H3 repertoire. This work was supported, in part, by NIH AI48115.

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THE SLE1, SLE2, AND SLE3 SUSCEPTIBILITY ALLELES DIFFERENTIALLY INFLUENCE THE DEVELOPMENT OF B CELLS FORCED TO EXPRESS ANTIBODIES WITH ARGinine-ENRICHED ANTIGEN BINDING SITES

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Purpose of Study: Systemic Lupus Erythematosus (SLE) is characterized by the production of pathogenic anti-DNA antibodies that can cause tissue injury. These anti-DNAs tend to encode arginine in their antigen binding sites. We previously generated a mutant immunoglobulin DH allele (ΔD-iD) that enriches for arginine in CDR-H3, which lies at the center of the antigen binding site. BALB/c mice expressing this altered DH demonstrate an increase in marginal zone (MZ) and a decrease in peritoneal cavity (PEC) B1 cell numbers. Both of these subsets have been linked to natural autoantibody production. Anti-DNA antibodies are easier to elicit in C57BL/6 mice, and the addition of the congenic alleles sle1, sle2, and sle3, each derived from either NZB or NZW mice, facilitates the development of SLE. We sought to determine whether the development of B cells expressing arginine-enriched antibodies is influenced by one or more of these sle alleles.

Methods Used: We backcrossed Δ D-iD onto C57BL/6; individually introduced sle1, sle2, or sle3; and then evaluated B cell numbers in the spleen and peritoneal cavity in comparison to wild-type.

Summary of Results: Relative to wild-type DH controls, Δ D-iD MZ cell numbers were significantly increased when in the presence of either the sle1 or sle3 alleles, but essentially unchanged when in the presence of sle2 or on the C57BL/6 background alone. In the peritoneal cavity, Δ D-iD B1a cell numbers were significantly decreased on the C57BL/6 background, and in the presence of either the sle2 or sle3 alleles. In the presence of sle1, Δ D-iD B1a cell numbers were maintained. Δ D-iD B1b cell numbers were also decreased on the C57BL/6 background and in the presence of sle3, but were unchanged in the presence of sle1 and sle2.

Conclusions: Thus, each sle allele variably influences the fate of B cells expressing charged antigen binding sites. This work was supported by NIH AI48115.

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CONTRIBUTION OF STRUCTURE TO IGE BINDING BY ARA H 2

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Purpose of Study: Ara h 2 purified from roasted peanut binds higher IgE levels than Ara h 2 from raw peanuts to determine if structural epitopes are more important than linear epitopes for IgE binding to Ara h 2, we assessed the denaturation of Ara h 2 over time with temperature and a reducing agent and compared the differences in IgE binding to the various folded and unfolded forms of this allergen.

Methods Used: Ara h 2 was purified from raw and roasted peanuts and IgE binding was compared. Also, raw Ara h 2 was treated with heat or a denaturing agent, dithiothreitol (DD, 2mM). IgE binding to the folded and unfolded Ara h 2 was compared using sera from peanut allergic and sensitized, but tolerant patients using western blot analysis. Circular dichroism (CD) was used to monitor the structural changes.

Summary of Results: Ara h 2 from roasted peanuts bind much higher IgE than raw peanuts. The structure of folded Ara h 2, which is predominantly alpha helical was very similar to Ara h 2 from roasted peanut. Ara h 2 was resistant to denaturation with heat, but was denatured after 24 hours incubation with DTT where the predominance towards alpha helical secondary structure shifts to random coil. The less structured Ara h 2, with reduced alpha helices, becomes the lower the level of IgE binding for majority of patients' sera.

Conclusions: The chemical modifications incurred by roasting are important IgE binding while in the raw conformational epitopes seem to be major contributors to IgE binding. Differences in IgE binding to various forms of Ara h 2 by allergic versus sensitized patient sera may be useful in development of more specific diagnostic tools.

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A COMPARISON OF OSTEOPOROSIS TREATMENT GUIDELINES, T-SCORE VS FRAX: DXA HAS LESS UTILITY IN NON-CAUCASIANS

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Purpose of Study: Osteoporosis (OP) is a major public health problem. Treatment for OP may be based on either BMD or fracture risk assessment (FRAX). These 2 methods may result in discordant treatment recommendations. The purpose of this study is to examine the characteristics of the discordant group.

Methods Used: A retrospective chart review was performed on consecutive DXA scans collecting data on patients with a BMD indicating OP (T-score ≤ -2.5 at any site). Individuals were separated into concordant (group A) and discordant (group B) groups with respect to FRAX treatment recommendations (treat if $>3\%$ hip or $>20\%$ major osteoporotic 10 yr fracture risk). Discordance was defined as a FRAX indicating no treatment when calculated either with or without femoral neck BMD (FN BMD).

Summary of Results: Data on 93 patients were analyzed. Group A had 44 patients: age 76 yrs, 93% Caucasian, 98% female. Group B had 49 patients: age 62 yrs, 47% Caucasian, 53% African American, 96% female. Group B had a higher hip but lower spine BMD, higher BMI (28.5 vs 24.6), were younger and more likely to be African American (all $p < 0.05$). Including FN BMD in FRAX led to different treatment recommendations in 20% of patients with T-score

defined OP (19/93). In group B, 11 out of 49 (22%) had concordant treatment recommendations when FN BMD was included in FRAX calculation but were discordant when FN BMD was excluded. Conversely, 8 out of 49 (16%) in group B were concordant only when FN BMD was excluded from FRAX calculation. Presence of fracture (OR=2.1 $p=0.01$) or parental hip fracture (OR=3.1 $p=0.02$) have increased likelihood of being in group A.

Conclusions: Patients with discordant treatment recommendations had fewer risk factors. Spine T-score was higher in the concordant group, probably due to degenerative changes related to the older age. African American race was the most predictive of discordance between the treatment guidelines. If FRAX is a more comprehensive predictor of fracture risk than T-score, since it considers multiple risk factors, then this study suggests that the recommendation for the need to perform a DXA in non-Caucasians and Caucasians should be different. These results have implications regarding the expense and utility of screening DXAs in non-Caucasians and is relevant to the current health debate.

Clinical Epidemiology and Preventive Medicine

Concurrent Session

1:00 PM

Saturday, February 27, 2010

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WAIST/HEIGHT MEASUREMENT VS BODY MASS INDEX IN RELATION TO RISK FACTORS IN BLACK AND WHITE CHILDREN: THE BOGALUSA HEART STUDY

JS. Mokha, P. DasMahapatra, W. Chen, SR. Srinivasan, J. Xu, GS. Berenson *Tulane University School of Public Health & Tropical Medicine, New Orleans, LA.*

Purpose of Study: Body Mass Index (BMI) is a convenient measure used to relate the impact of obesity with cardiovascular (CV) risk factors. However, BMI does not always reflect central obesity and it progressively increases from childhood to adolescence whereas Waist/Height Ratio (WHR) is a relatively constant measure with 0.5 as a usable cut point to define abdominal obesity. The current study compares these two measures with regards to their relation to CV risk factors.

Methods Used: A cross sectional survey of CV risk factors data on 3238 children (55% whites and 49% blacks) 4-18 years of age was used. The subjects were further categorized into three age groups (4-8, 9-14, 15-18 years). Race- and sex- correlation analysis were performed. Correlation coefficients using WHtR and BMI were compared.

Summary of Results: BMI showed an increase across the three age groups whereas the WHtR did not significantly change, with a mean of 0.46. White males had significantly higher WHtRs after adjusting for age ($p < 0.05$). Except for height, Pearson correlations for other anthropometric indices on the total population were significantly associated with WHtR ($p < 0.0001$), with BMI and subscapular skinfold thickness showing the strongest correlations across all race-sex groups. On comparing the Pearson coefficients for WHtR and BMI, WHtR showed significantly higher correlation with total (0.140 vs. 0.037, $p < 0.0001$) and LDL cholesterol (0.194 vs. 0.079, $p < 0.0001$) whereas BMI was more strongly associated with various risk factors that included systolic and diastolic blood pressures, insulin and insulin resistance index (HOMA-IR) ($p < 0.0001$), potentially more related to the cardiometabolic syndrome.

Conclusions: WHtR and BMI are highly correlated with CV risk factors; BMI being a better predictor of blood pressures, insulin levels and HOMA-IR, and WHtR of serum total and LDL cholesterol.

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TRANSMISSION DYNAMIC OF A NOVEL INFLUENZA A (H1N1) OUTBREAK IN A SUMMER CAMP

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Purpose of Study: To analyze a novel H1N1 influenza outbreak pattern in a summer camp for children with hematologic and oncologic conditions.

Methods Used: In July 2009 an outbreak of H1N1 influenza occurred at a summer camp attended by 101 campers with ages ranging from 5 to 15 years (children with hematologic and oncologic conditions and healthy siblings) and 116 staff (healthy or with similar medical problems). The campers and some

staff were divided into eight groups ("patrols") by age and gender (G1 being youngest females and B4 being oldest males). The patrol members spent all of their time together (eating, sleeping, and camp activities). After the camp closing, questionnaires were sent out to all camp participants to identify subjects with symptoms of influenza-like illness which were developed within 10 days after closing of the camp. A possible outbreak pattern was proposed with a consideration of interactions within and between patrols and siblings, and the date that symptoms first appeared. The attack rates for each camp patrol (the percentage of cases per number of subjects in each patrol who completed the questionnaires) were calculated and compared.

Summary of Results: Eighty-eight staff (76%) and seventy-seven campers (76%) completed the questionnaire. On the second day of camp one unassigned female staff, a G3 camper, and a G3 staff were the first cases to report symptoms consistent with H1N1 infection. During the 4 days of camp and the 10 days after, 59 cases (36 campers and 23 staff) were identified. The order of patrols from highest attack rate to lowest was G1 (54%), B2 (50%), G3 (46%), G4 (42%), G2 (41%), B3 (36%), B1 (29%), and B4 (18%).

Conclusions: The staff members without a patrol assignment who interacted with multiple patrols, common camp activities, and sibling interactions may have contributed to transmission between the patrols, while shared schedule and physical closeness may have led to transmission within a patrol. The attack rates were higher in the patrols with younger campers, and female campers. The low attack rate in B1 patrol may be due to special precautions placed on the patrol because of a camper with ventriculoperitoneal shunt.

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REVISION TOTAL HIP ARTHROPLASTY IN THE GERIATRIC PATIENT: IS IT ANY DIFFERENT FROM YOUNGER PATIENTS?

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Purpose of Study: Revision total hip arthroplasty (THA) has been estimated to increase nearly 200% over the next 20 years. Increasing numbers of geriatric patients will require this complex operation. The purpose of this study was to evaluate whether there was any difference(s) in the outcome following revision THAs between geriatric and younger patients.

Methods Used: This was a retrospective review of consecutive patients who had undergone revision THAs under the same surgeon from 2004 to 2008. 25 patients older than age 75 years (mean age of 80 years) underwent 28 revision THAs. These patients were matched to another 28 younger patients less than age 70 years (mean age of 58 years) who had undergone revision during the same time interval. There were 32 females and 21 males. Matching was done with regard to gender, medical co-morbidities, type of operation, implants, surgical techniques, and postoperative and rehabilitation protocol. Outcome measures included: Harris hip score, intraoperative blood loss, length of stay, and complications. Statistical analysis was done using student t tests.

Summary of Results: All patients had minimum 1 year follow-up (mean 16 months for the geriatric group and 24 months for the younger group). All patients in both groups were under the consultation of a hospitalist during hospitalization. There was no difference in the Harris hip score (91.3 for geriatrics vs. 90.2 for younger, $p > 0.05$). Intraoperative blood loss was similar between the geriatric and younger groups: 915ml and 930ml, respectively ($p > 0.05$). Overall complication rate (surgical and non-surgical) was 39% for the geriatric group and 36% for the younger patients ($p > 0.05$). The only difference among the outcome measures was in the length of stay: 6.2 days (± 2 days) for the geriatric group vs. 5.5 days (± 1 day) for the younger group ($p = 0.03$). No patients died during the follow-up period.

Conclusions: We found no difference in outcome between the geriatric and younger groups except for length of stay. This could be a reflection of achieving physiotherapy goals more slowly, longer duration of monitoring of medical conditions, or other factors. We continue to extract more data from chart review, including cost analysis. We believe complex revision THAs can be safely performed in geriatric patients with equally satisfactory outcome.

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THE ROLE OF DIETARY DIVERSITY IN THE NUTRITIONAL STATUS OF SCHOOL-AGED CHILDREN IN RURAL HONDURAS

M. Gourley¹, G. Winters¹, J. Anderson¹, R. Smalligan² ¹East Tennessee State University, Johnson City, TN and ²Texas Tech Univ Health Sciences Center, Amarillo, TX.

Purpose of Study: Studies in developing countries have shown that increased diversity in diet increases the likelihood that adequate amounts of nutrients critical for the growth of a child will be consumed. The objective of this study was to determine the prevalence of malnutrition among rural Honduran children and to determine if dietary diversity in these 8 and 9-year-old children correlated with their nutritional status as measured by body mass index (BMI) (kg/m²).

Methods Used: A random sample of 8 and 9-year-olds was chosen from 14 schools in three communities in rural Honduras. Parents completed a survey, based on those used by USAID, with questions about food groups consumed within the past 24 hours and indicators of socioeconomic status. Results were analyzed using Chi-Square and t-tests.

Summary of Results: 127 of 181 eligible students were surveyed (72.9%). 62 boys and 65 girls participated. Height and weight measurements were used to calculate each child's BMI, and these were compared to current WHO growth parameters. Only 3 percent of children were classified as malnourished and 4 percent as having stunted growth. Individual dietary diversity scores (IDDS) ranged from 3-8 with a mean score of 5.5. No correlation was found between IDDS and BMI in either gender or age group. However, a significant positive correlation ($p = 0.04$) was shown between those who reported eating beans or legumes and BMI.

Conclusions: A high prevalence of malnourished children is common in developing countries; however, this study showed few malnourished children in the communities studied. An IDDS of 4 or higher generally indicates an adequate diet, hence the mean IDDS of 5.5 showed that the children had access to a variety of foods. The lack of correlation between BMI and IDDS was inconsistent with prior studies, most likely due to the low prevalence of malnutrition in the study group. Few studies exist linking socio-economic status and dietary diversity, and this study demonstrated no such correlation. The positive and statistically significant correlation between legumes and BMI suggests that legume consumption could serve as an indicator of adequate nutritional intake by children and should be further studied in the future.

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PSORIASIS AND CARDIOVASCULAR RISK FACTORS: A U.S. POPULATION-BASED CROSS-SECTIONAL STUDY

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Purpose of Study: Previous research exploring the associations between psoriasis and cardiovascular risk factors is quite conflicting, and most studies were either hospital-based or were performed on populations outside of the United States. U.S. population-based data regarding the associations between psoriasis and cardiovascular risk factors are not readily available. The current study seeks to determine whether there are associations between psoriasis and cardiovascular risk factors on a nationwide level.

Methods Used: A cross-sectional study was performed using data from the National Health and Nutrition Examination Survey (NHANES) from 2003 through 2004, consisting of a probability sample of the U.S. population aged 20 to 59. Descriptive statistics of the study population ($n = 3138$) were summarized, and associations between psoriasis and the cardiovascular risk factors were tested using the chi-square test for categorical variables and the t-test for continuous variables. Multivariate logistic regression modeling was performed to determine which cardiovascular risk factors are independently associated with psoriasis.

Summary of Results: The demographics of the study participants with psoriasis ($n = 144$) and without psoriasis ($n = 2994$) were summarized descriptively. Unadjusted, bivariate analyses showed that the study participants with psoriasis were significantly more likely to be older, male, white, and obese and to have the metabolic syndrome, hypertension, a reduced HDL-C, and a history of any cardiovascular disease. After adjusting for each of these covariates, only white race remained statistically significantly associated with having psoriasis. Furthermore, after adjusting for the above listed covariates and stratifying by gender, none of the covariates were statistically significant in either the male group or the female group.

Conclusions: The results of this study suggest that psoriasis is not associated with cardiovascular risk factors or with a history of cardiovascular disease. Nonetheless, the study was limited by its small sample size and its age restriction, and additional studies examining a larger sample of the U.S. population are warranted.

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PREVALENCE OF STAPHYLOCOCCUS AUREUS NASAL CARRIAGE IN PHYSICIANS-IN-TRAINING

RS. Gusso¹, V. Hsu¹, MC. Bowman¹, KS. Yee¹, C. Mancero², T. Williams³, R. Gomez¹, N. Saleh², G. Everett¹ ¹Florida Hospital, Orlando, FL; ²Florida Hospital, Orlando, FL and ³Florida State University College of Medicine, Orlando, FL.

Purpose of Study: Physicians in training are frequently exposed to Staphylococcal infections but little is known about the prevalence of methicillin-resistant *S. aureus*(MRSA) and methicillin-sensitive *S. aureus* (MSSA) colonization or infections in these physicians. Obtaining a better understanding of this prevalence may eventually help to devise strategies to combat the carrier state or diminish the impact that carriers have in healthcare setting.

Methods Used: All current Florida Hospital residents were invited to participate in the study. Each participant is screened by nasal culture for MRSA and MSSA every six months until they complete their residency or 3 years. Each year the point prevalence will be determined as well as tracking of individuals for acquisition or loss of MRSA/MSSA over time. Questionnaires at entry and every six months will evaluate demographics, infection history, and clinical rotations. At years 2 and 3 a multivariate analysis of data will determine if there is an association between organism acquisition and specific rotations or demographic characteristics.

Summary of Results: Of 117 current residents, there were 83 participants from Internal Medicine, Emergency Medicine, General Surgery, Geriatrics, and Podiatry. Initial screening revealed twenty-five were positive for MSSA and none were positive for MRSA. At the onset of the study, the point prevalence for MRSA and MSSA was 0 and 0.30, respectively. Of the eighty-three screened, four documented prior personal staphylococcal infection, one with MRSA, one with MSSA, two with unknown species.

Conclusions: The prevalence of *S.aureus* carrier state was similar to that in the general population. The lack of any positive MRSA carriers was surprising. Follow up point-prevalence surveys will allow us to track acquisition or loss over time and to assess the possible relationships to demographics and clinical rotations. It also implies that a significant percentage of physicians in training may be staphylococcal carriers and not know it.

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THE EFFECT OF A CHLORHEXIDINE BATH ADMISSION PROTOCOL ON PREVENTION OF NOSOCOMIAL METHICILLIN-RESISTANT STAPHYLOCOCCAL AUREUS INFECTIONS

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Purpose of Study: Nosocomial (healthcare-associated) methicillin-resistant Staphylococcal aureus (MRSA) infections are an increasing problem nationwide. While randomized controlled trials support the use of local chlorhexidine (CHG) for preventing infections following placement of invasive devices, the use of CHG bathing pre-operatively or in ICU patients has had limited and variable support from mostly non-randomized cohort studies. This study investigates whether applying a CHG bath protocol to all patients admitted to a community hospital decreases the incidence of nosocomial MRSA infections.

Methods Used: A retrospective cohort analysis of nosocomial MRSA infections was performed at a community hospital before and after a protocol to provide full body CHG baths to all patients on admission was implemented. Adult patients in the six months before the protocol were compared with patients 6 months after, excluding a 2 month startup period to allow the policy to take full effect. This is an intent-to-treat analysis.

Summary of Results: Twenty patients out of 11,373 admissions, 0.18%, developed nosocomial MRSA infections prior to CHG implementation, compared with 25 out of 11,599 admissions, 0.22%, after the initiative ($p < 0.49$). MRSA wound infections were most common, followed closely by pneumonia. The groups were similar in regards to age, 67 vs. 65, and ethnicity. Patients in the intervention group had a shorter length of stay preceding infection, 14 days vs. 16 days, and a higher proportion of males, 64% vs. 40%. Protocol adherence was a significant issue; a random chart review of 308 patients showed 52% adherence (95% CI, 47% to 57%).

Conclusions: Our analysis indicates a hospital-wide protocol to administer CHG baths to all patients did not reduce nosocomial MRSA infections. Poor adherence limits the interpretation of the CHG effect, but needs to be considered given the time involved and its inconvenience to the patient. Additional studies incorporating randomization and methods to improve adherence are needed to determine the efficacy of the CHG baths.

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RECIDIVISM RATES OF TEEN DRIVING TRAUMA PREVENTION PROGRAM IN BIRMINGHAM, ALABAMA

TM. Galey, G. Smith *University of Alabama at Birmingham, Birmingham, AL.*

Purpose of Study: To determine the recidivism rates of teenagers who participated in the Teen Driving Trauma Prevention course between 1997–2000.

Methods Used: The program was begun in Birmingham, Alabama in 1997 as an alternative court sentencing for teen drivers who commit minor to moderate offenses. The attendees attend a half day course at the Children's Hospital of Alabama which includes a lecture from local law enforcement, a viewing of a mock trauma then "following the patient" to the Pediatric Intensive Care Unit for a tour and ends with a sit down session with a family who lost a teenage child due to reckless teen driving.

All court records for participants were accessed from the years 1997–2000 using the participants name and case number. All driving offenses occurring after the participants' completion of the program were recorded. Information about repeat offenses could not be located in the court database for 16 total attendees. The recidivism rates were calculated based on the number of attendees for each calendar year which had information still present in the court system and then divided by the number of individuals recorded to have a driving offense.

Summary of Results: Yearly recidivism rates are enclosed in table 1 with a yearly average of 19% for the years 1997–2000. We reviewed the court records of 204 attendees and found that 7 (3%) of the participants had committed 2 or more repeat offenses since completing the program. Speeding was the most common repeat offense 27/40 (67%).

Conclusions: After reviewing court records of 204 participants we found a recidivism rate of 19%. Other studies of similar programs have reported recidivism rates of 28–42%. While there are many areas we can still improve, we feel this program is a helpful tool in helping to decrease teen driving accidents and fatalities.

Recidivism Rates

Year	Total Attendees (Records Available)	Total Re-offenders	Recidivism Rate
1997	56 (50)	11	22%
1998	54 (51)	10	20%
1999	60 (56)	14	25%
2000	50 (47)	5	10%
Total	220 (204)	40	19%

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ANALYSIS OF CHILD PASSENGER SAFETY IN PATIENTS OF A PEDIATRIC EMERGENCY DEPARTMENT

A. Cease², K. Monroe¹ ¹Univ of Alabama, Birmingham, AL and ²Univ of Alabama, Birmingham, AL.

Purpose of Study: To determine the number of children properly restrained during transit to a pediatric Emergency Department (ED) for care. To ascertain parental knowledge of Alabama Laws and American Academy of Pediatric (AAP) guidelines and where they obtain this information.

Methods Used: An ED (patient care rooms) waiting area, convenience sample of Alabama parents who have children ≤ 13 years of age were surveyed over a five week period. Appropriate use of CPS restraints was determined using Alabama law and AAP recommendations. Use of Car Seat Checks provided by Children's Hospital and Safe Kids, knowledge of Alabama laws and CPS guidelines and the source of information used by parents were ascertained.

Summary of Results: Among 525 patients identified, 520 (99.0%) participated. Appropriate use per Alabama Law and AAP guidelines was 72.3% and 60.6%, respectively. 5.0% were unrestrained. Booster seats were the most commonly misused restraint. Car seats were reportedly used correctly 81.9%. Parents who had used the Car Seat Checks program had

(correct booster seat and car seat use rates of 95.8% and 61.5% respectively. Unfortunately, only 31.2% of patients had knowledge of the Car Seat Checks program and only 40.6% knew the current law. Most often parents stated that the hospital where their child was born was the primary (and sometimes only) source of CPS information.

Conclusions: This study illustrates the need for improving parental knowledge of appropriate child passenger restraint use, (especially booster seats) and car seat checks programs. Car seat program assistance is associated with high levels of appropriate use.

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SELF-REPORTED ADHERENCE TO ANTI-DIABETIC MEDICATIONS IS ASSOCIATED WITH GLYCEMIC CONTROL IN PATIENTS WITH TYPE 2 DIABETES

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Purpose of Study: Self-report questionnaires can be convenient tools for assessing anti-diabetic medication adherence in outpatient practices. To determine the usefulness of 2 self-report adherence scales in the clinical setting, we examined the association between anti-diabetic medication adherence scale scores and glycemic control in patients with type 2 diabetes.

Methods Used: Patients were recruited from an endocrinology clinic. Adherence to anti-diabetic medications was assessed using the eight-item Morisky Medication Adherence Scale (MMAS-8) and the 9-item Hill-Bone Medication Compliance Subscale (HBCS). Patients' hemoglobin A1C (A1C) values closest to the survey date were abstracted from electronic medical records. Low, medium, and high adherence to diabetes medications were defined as scale scores <6, 6-8, and 8 on the MMAS-8, and >11, 9-11, and <9 on the HBCS. Poor glycemic control was defined as A1C ≥ 9%.

Summary of Results: The mean age of the 230 participants was 60.7 ± 12.3, 43% were male, 39.0% were black, 66.5% had body mass index (BMI) ≥ 30, 29.0% had poor glycemic control, and 31.7% (MMAS-8) and 37.0% (HBCS) had low adherence to anti-diabetic medications. Cronbach's alpha values were .70 for MMAS-8 and .63 for the HBCS, and the two scales were correlated with each other (Spearman's $r = -0.65$, $p < 0.001$). On both scales, low adherence was associated with poor glycemic control. After adjustment for age, race, gender and BMI, patients with low levels of medication adherence on the MMAS-8 and HBCS were 1.4 (95% CI 1.1, 1.7) and 2.0 (95% CI 1.2, 3.4) times, respectively, more likely to have poor glycemic control, compared to those with high adherence.

Conclusions: We identified a significant association between low anti-diabetic medication adherence and poor glycemic control using 2 self-report medication adherence tools. These tools may be useful for assessing patients' adherence to anti-diabetic medications in the outpatient setting.

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A STUDY ON THE TRENDS OF HOSPITAL ACQUIRED INFECTIONS IN MOBILE, ALABAMA

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Purpose of Study: Hospital acquired infections (HAIs) sometimes referred to as nosocomial infections are infections that a patient acquires during treatment or while being hospitalized. It has been estimated that every year approximately two million patients experience and suffer from a nosocomial infection and as a result more than one hundred thousand of these patients die. This research was aimed at determining prevalent practices for preventing hospital acquired infections at local hospitals in Mobile, AL and to assess awareness of the problem in lay public.

Methods Used: Infection control personnel at five major hospitals were interviewed in the city of Mobile between the dates of May 28, 2009 and June 23, 2009. Three hundred and seventy participants from the general public in Mobile, AL responded to a survey study to determine the public knowledge, awareness, opinions and interests of HAIs in Mobile.

Summary of Results: The hospital interviews revealed that nosocomial infections were being prevented using the bundling of evidence based practices, isolation of patients based on symptoms (not positive blood cultures), and stressing the importance of hand washing. The survey revealed that citizens of Mobile were interested in knowing the rates of nosocomial

infection at local hospitals, and this information would influence their choice of hospital for treatment in 93.8% cases. Interestingly, even though they agreed handwashing was an important precaution to prevent infection only 18% reported asking their healthcare provider to wash their hands before examining or treating them.

Conclusions: Hospital acquired infections are a source of morbidity and mortality for the consumer and an additional health care cost burden for hospitals and the health insurance industry. The capabilities of infection control are changing and advancing every minute. A greater transparency in nosocomial infection rates at local hospitals may enhance infection control measures at these hospitals and hence enhance care and reduce health care costs for the consumers.

Gastroenterology and Clinical Nutrition II Concurrent Session

1:00 PM

Saturday, February 27, 2010

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INTERSTITIAL CELLS OF CAJAL (ICC) AND NERVE FIBER CHANGES IN THE GASTRIC MUSCLE OF PATIENTS WITH DIABETIC GASTROPARSIS

C. Subramony, J. Hughes, C. Lahr, D. Spree, S. Bigler, T. Abell *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: Normal gastric motility depends upon smooth muscle cells richly supplied by a network of neuronal cell processes from the nerve plexuses and the interstitial cells of Cajal (ICC) which in smooth muscle relay electric impulses from the inter-muscular plexus to the smooth muscle cells, thereby modulating gut motility. Animal studies have shown reduced numbers of ICC in gastroparesis. Here, the number of ICC and neuronal cell processes observed in gastric biopsies from patients with diabetes (DM) and gastroparesis (GP) was compared with those seen in gastric tissues obtained post-mortem.

Methods Used: Full-thickness gastric biopsies were obtained from thirty patients (23 w, 7 m; mean age of 49.8 yrs) with drug-refractory DM GP during surgery to implant a permanent gastric electrical stimulator and gastric tissues were obtained from 19 control patients post-mortem (6 w, 13 m, mean age of 43.6 yrs; includes 1 w and 1 m with DM). Immunostains with antibodies directed against CD117 (for ICC) and S-100 protein (for neuronal processes) were performed on paraffin-embedded sections. Cells in the outer and the inner muscular layers were counted in ten high power fields (x400 magnification). The mean number of cells per high power field was calculated.

Summary of Results: Our findings differed from those reported for animal studies (Table 1). The number of CD117 cells did not differ between groups. However, significantly fewer S-100 positive nerve fibers were seen in samples from DM GP patients. [Table 1]

Conclusions: Patients with diabetic gastroparesis had significantly fewer nerve fibers in both the inner and outer muscle layers than non-gastroparetic controls. ICC were seen in greater numbers in the inner muscle layer of diabetic patients with gastroparesis than were seen in control patients. Further studies correlating histologic changes with direct gut electrophysiology may reveal clinically useful information.

TABLE 1

	Diabetics	Control	P value
S-100 outer Muscle	6.3	20.7	0.00001
S-100 Inner Muscle	13.4	26.1	0.009
CD117 Outer Muscle	5.36	6.97	0.42
CD117 Inner Muscle	9.9	6.67	0.025
Ratio CD117/S100 outer muscle	1.49	0.427	0.008
Ratio CD117/S100 inner muscle	1.07	0.364	0.003

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GASTRIC ELECTRICAL RESPONSE TO DIFFERENT STIMULATION PARAMETERS

S. Dharam, C. Lahr, D. Spree, J. Hughes, T. Abell *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: For patients with refractory gastroparesis, permanent gastric electric stimulation (GES) has emerged as an effective treatment over

the last two decades. In the past, low-energy level stimulation was largely used; however, with increasing patient experience, we realized that some patients respond better to higher energy stimulation. This study was performed to evaluate the effect of changing energy levels upon electro-gastrogram (EGG) parameters such as frequency, amplitude and frequency-amplitude ratio (FAR).

Methods Used: The study participants include nineteen patients who underwent placement of permanent gastric electrical stimulator. At the time of placement of the stimulator, the surgical team measured the EGG parameters at baseline with the stimulator off, then at low, medium and high-energy settings and then with the stimulator off again.

Summary of Results: The mean values for the EGG parameters obtained at the different energy settings are summarized in the table below.

Conclusions: EGG obtained after GES demonstrates immediate improvement in frequency, amplitude and FAR. Though the low energy settings were most effective in improving EGG parameters in 10 patients, medium or high-energy settings proved to be more effective in achieving a lower FAR in 9 patients. These findings indicate that the method of action of GES may be immediate local improvement of gastric electrical activity. Stimulation parameters resulting in maximal improvement in EGG parameters may differ between individual patients.

Energy Level EGG Parameter	Baseline	Low	Medium	High	Post-GES
Mean Frequency	4.80	4.39	4.32	4.95	4.60
Mean Amplitude	0.21	0.44	0.30	0.32	0.29
Mean FAR	40.90	17.02*	20.18	29.43	27.11

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LENGTH OF HOSPITALIZATION IN GASTROPARESIS

T. Vesa, A. Kedar, C. Lahr, T. Abell *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: At UMMC, the majority of Gastroparetic (GP) patients seen have medication-refractory GP in need of permanent Gastric Electrical Stimulators. We conducted a quantitative analysis of length of hospital stay related to Gastroparesis.

Methods Used: A pre-existing gastric stimulation database To The Limit (TLL) database was utilized. It includes 98 patients with gastroparesis admitted to University of Mississippi Medical Center (UMMC) Hospital from September of 2007 till July 2009. We calculated the number of admissions for elective Gastric Electrical Stimulator (GES) placement, readmissions, complications related and non-related to the surgical procedure, associated number of co-morbidities and how these parameters affect LOS (Length Of hospital Stay).

Summary of Results: Ninety-eight patients were admitted 172 times since September 2007. The total average LOS was 9 days per patient. Elective admissions for permanent GES placement were 101 (59% with average LOS of 11 days): 71 occurred without complications with average LOS of 7 days; 30 occurred with complications with LOS of 21 days - none of these complications were directly related to the procedure. The remainder of the admissions due to non-elective reasons, which correspond to 71 (41%) admissions with average LOS of 5 days. After elective GES placement, there were 68 readmissions and only 7 were triggered by post-operative complications with LOS 4.5 days.

Conclusions: In general, gastroparesis hospitalizations are very often accompanied by complications due to the long list of potential co-morbidities carried by these patients as well as due to the difficulty in effectively controlling severe pain, nausea and vomiting. In a gastroparesis referral center. These summation factors contributed to the length of hospital stay that extends beyond a previously established national average of 6.1 days*.

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RELATIONSHIPS BETWEEN PSYCHOLOGICAL STRESS, GASTROINTESTINAL SYMPTOMS AND PHYSIOLOGY, IMMUNE FUNCTION AND COAGULATION IN PATIENTS WITH GASTROPARESIS (GP) AT TEMP GES

R. Vance, A. Kedar, J. Hughes, D. Spree, M. Griswold, G. Marshall, T. Abell *University of Mississippi Medical Center, Jackson, MS.*

Purpose of Study: We evaluated the baseline relationships between psychological stress, upper gastrointestinal symptoms and physiology, cytokine levels, and coagulation measures prior to implantation of a temporary gastric electrical stimulator (GES) and compared these baseline values to measures obtained on day five of the temporary GES.

Methods Used: We examined 14 consecutive patients (2m, 12f, 3 African American, 11 white), mean age of 46 years, each with the diagnosis idiopathic (n=7), post-surgical (n=3) or diabetic (n=4) GP. Measures of upper GI symptoms (nausea, vomiting, anorexia/early satiety, bloating and total symptom scores (TSS), gastric emptying times, coagulation measures and psychological stress quantified by the Perceived Stress Scale (PSS).

Summary of Results: The variable means from visit one and visit two along with t-test p values are summarized in table 1.

Conclusions: Changes in vomiting secondary to temporary GES appear to correlate with changes in EGG ratio, upper GI symptoms, Tregs levels and coagulation measures in this small sample of GP patients status post temporary GES. Further study could provide clearer definition to these complex relationships.

Variable	Mean at visit 1	Mean at visit 2	p value
Nausea	3.461538	1.730769	0.006914
Vomiting	2.692308	1.461538	0.074576
Anorexia	3.041667	2.076923	0.06881
Bloating	3.208333	1.692308	0.013436
Abdominal pain	2.75	1.384615	0.044671
TSS	15.38462	8.269231	0.00428
EGG freq (all)	6.453571	5.959231	0.673355
EGG amp (all)	0.694286	0.990769	0.394257
EGG ratio (all)	26.42536	11.48731	0.082786
EGG freq (<3.3 cpm)	3.06	7.29	0.0346
GET tot (all)	109.0385	120.55	0.66596
GET tot (Rapid)	52.68333	102.0833	0.095824
CRP	1.066667	1.933333	0.499305
Fibrinogen	393.8462	449.2727	0.276272
R5 (Tregs)	3.075385	2.959231	0.829935
PSS	23.93	23.93	0.701

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IS COLONOSCOPY A VALID TIME TO SCREEN FOR DIABETES MELLITUS?

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Purpose of Study: To evaluate the efficacy of opportunistic screening for diabetes mellitus at the time of colonoscopy in asymptomatic individuals who have risk factors for developing diabetes mellitus.

Methods Used: We performed a retrospective chart review of 100 consecutive outpatient colonoscopies. Patient data and characteristics were reviewed to identify those who met criteria for diabetes screening as per guidelines from the American Diabetes Association and American Association of Clinical Endocrinologists.

Summary of Results: The average age was 54 with screening colonoscopy and rectal bleeding being the most common reasons for evaluation. 59 asymptomatic patients met criteria to screen for diabetes mellitus. The major risk factor identified was obesity with an average BMI of 31. Most of these patients were endoscopic naïve (75%;44/59) and with no record of a fasting blood glucose within the last year (85%;50/59).

Conclusions: Colonoscopy is an ideal time and opportunity to screen for diabetes mellitus in appropriately selected patients.

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SLOW TRANSIT CONSTIPATION IS ASSOCIATED WITH ABNORMAL NEURONAL NETWORKS

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Purpose of Study: The colonic neuronal morphology of patients with chronic constipation has not been well characterized. We compared the histology of 7 patients status post colectomy for intractable constipation with 4 controls, to better define these abnormalities. 7 patients [age range, 15-54,

all females] with chronic constipation were compared with 4 matched controls [age range, 42-49, all females].

Methods Used: Colectomy specimens and normal controls were evaluated by identical methods. Immunostains with antibodies directed against CD117 (for ICC, interstitial cells of Cajal) and S-100 protein (for neuronal processes) were performed on paraffin-embedded sections. Cells in outer and the inner muscular layers were counted in ten high power fields (x400 magnification). The mean per high power field was calculated, as well as the average of the inner and outer muscle layers. Results were compared by t-test.

Summary of Results: Compared to controls, the CD-117 cells were lower for the outer muscle layer but the results were not statistically significant. The S-100 cells in the inner muscle layer and the average for combined inner and outer S-100 cells were significantly lower in patients vs. controls (see table below).

Conclusions: In this sample of patients undergoing colectomy vs. controls, both CD-117 (Cajal) and S-100 (Neural) cells are abnormal with the greatest abnormality being the neural cells. Emerging neuro-muscular staining techniques and electrophysiology may offer additional understanding of intractable chronic constipation.

Colectomy versus Controls

	CD117 Outer	CD117 Inner	CD117 Average	S100 Outer	S100 Inner	S100 Average
Colectomy Patients Mean	4.98	6.3	5.64	12.9	41.22	27.09
Controls Stan Dev	3.77	5.71	4.74	13.66	36.93	24.75
Controls Mean	8.6	7.85	8.28	17	90.75	53.87
Controls Stan Dev	4.42	3.43	3.51	8.85	18.29	8.31
T test P values	0.37	0.62	0.37	0.60	0.02	0.04

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HOW EFFECTIVE AND SAFE IS GASTRIC ELECTRICAL STIMULATION FOR GASTROPARESIS: 10-YEARS OF EXPERIENCE

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Purpose of Study: Enterra Therapy, providing gastric electrical stimulation (GES) to control GI symptoms in severe, diabetic (DM), idiopathic (ID) and post-surgical (P-S) drug-refractory gastroparesis (GP), is recognized as an effective treatment option. The long-term observations of GES efficacy, complications, and patients' management have been sparsely reported. This study was designed to assess long-term clinical outcome of GES therapy, in a large cohort of patients.

Methods Used: 221 GP patients (142 DM, 48 ID and 31P-S) with GES therapy for one to 11 years were assessed. 164 (74%) were F, median age of 38 y (18-70). The median duration of DM was 18 y (range: 1-41). Total symptom score (TSS) of typical GP symptoms were evaluated by using a 5-point scale. The gastric retention test (GR), nutritional status, weight, days of hospitalizations, the use of GP medications, HbA1c and adverse events was evaluated at baseline and at F/U.

Summary of Results: Out of the 221 GES patients, 188 had F/U data available for at least 1 year (mean: 56 months, 12-131). Days of hospitalization went down from mean 41 to 6, and the use of medications was also reduced ($p < 0.05$). The mean reduction of TSS in the DM patients was greater than in ID and P-S groups (55% vs. 47% vs. 48%). More patients with DM (60%) and P-S GP (59%) had > 50% reduction in TSS than ID (49%). More ID continued the supplemental nutritional support. Weight significantly increased in all groups (from 113 to 127lbs). At F/U, all groups, had similar, although abnormal, GR results (mean retention at 2h-64% and at 4h-30%). Overall, 26 patients (12%), 23 DM and 3 ID died of non-GES therapy related causes, 20 cases were due to complications of DM. Also, 24 patients (11%) had their devices removed with 13 cases being related to infection of the pocket. No technical malfunctions of the System were observed.

Conclusions: 1) Enterra significantly improved subjective and objective parameters, with efficacy of GES sustained for >10 years; 2) Patients with DM and P-S GP benefited more than patients with ID GP; 3) There was a good safety and tolerability profile. 4) Physicians need to be aware of this novel therapy, since Enterra patients will be increasingly seen in their practices.

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BASELINE RELATIONSHIPS BETWEEN PSYCHOLOGICAL STRESS, IMMUNE FUNCTION, IN PATIENTS WITH GASTROPARESIS

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Purpose of Study: Purpose of study: Gastroparesis (GP) is a gastric motility disorder known to cause many upper gastrointestinal symptoms which can create significant psychological stress in affected patients. GP patients have also been shown to have hypercoagulable risk factors associated with certain cytokine imbalances believed to cause immune dysregulation. We evaluated the baseline relationships between psychological stress, upper gastrointestinal symptoms and physiology, cytokine levels, and coagulation measures prior to implantation of a temporary gastric electrical stimulator (GES).

Methods Used: We examined 14 consecutive patients (2m, 12f, 3 African American, 11 white), mean age of 46 years, each with the diagnosis idiopathic ($n=7$), post-surgical ($n=3$) or diabetic ($n=4$) GP. Baseline levels of upper GI symptoms (nausea, vomiting, anorexia/early satiety, bloating and total symptom scores (TSS), mucosal electrogastragrams (frequencies, amplitudes, and ratios), gastric emptying times (1hr, 2hr, 4hr and total), Tregs, coagulation measures (CRP, fibrinogen), and psychological stress quantified by the Perceived Stress Scale (PSS) were obtained and analyzed through regression models for any correlations.

Summary of Results: Mean values for baseline variables are summarized in table 1. Data were analyzed by regression analyses and showed that, at baseline, PSS was found to correlate with vomiting ($p < 0.0001$) and TSS ($p < 0.05$), respectively, with borderline correlation to nausea ($p = 0.08$). There was no statistically significant correlation between Tregs and PSS after regression analysis but a borderline correlation was found between baseline Tregs and vomiting ($p = 0.071$).

Conclusions: In our small sample of GP patients, baseline elevations in both vomiting scores and total symptom scores correlate with higher levels of psychological stress quantified by PSS scores.

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EVALUATION OF AUTONOMIC AND VAGAL NERVE FUNCTION IN ADULT PATIENTS WITH CYCLIC VOMITING SYNDROME

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Purpose of Study: Cyclic vomiting syndrome (CVS) in adults is a disorder characterized by recurrent and stereotypic episodes of severe nausea and vomiting separated by symptom-free periods. Autonomic and vagal nerve dysfunction has been a postulated mechanism for the pathogenesis of this disorder in children but this has not been investigated in adult CVS.

Methods Used: The parasympathetic nervous system was tested through heart rate response to deep breathing [expiration/inspiration (E/I)], valsalva and posture indexes and the sympathetic nervous system was evaluated through postural changes in heart rate and blood pressure and sympathetic skin response in the hand and foot in 22 adult patients (18 M), mean age 40 ± 5 (range 19-61 yr) with CVS. Abdominal vagal nerve function was evaluated with a standard sham meal test to stimulate pancreatic polypeptide (PP) in 9 of the patients (6 female, mean age 38 ± 4). A 4-hr standard radionuclide gastric emptying test (GET) was performed in all patients to measure the percent of gastric retention at 0, 1, 2, 3 and 4 hr and defined as normal, rapid and slow.

Summary of Results: Parasympathetic abnormalities were elicited as orthostatic tachycardia in 2 patients (mean HR increase 42 beats/min) and a decline in BP in 5 patients (mean BP drop 25 mmHg). 5 patients had an abnormal response to deep breathing and E/I index < 1.20 . Sympathetic nerve dysfunction was reported in 7 patients with absent sympathetic skin response in the foot and/or hand. 4 patients had abnormal sham meal response defined as failure of Plasma PP levels to increase by > 25 pg/ml suggesting abdominal vagal dysfunction. 2 of these patients with abnormal PP response also had had abnormal parasympathetic test. Gastric emptying results were similar in both groups of normal and abnormal PP and also between normal the impaired autonomic function groups.

Conclusions: 1) Overall 45% of patients had autonomic dysfunction. 2) Overall 23% had abnormal parasympathetic function including 44% (4/9) with impaired vagal nerve function. These observations raise the question of both autonomic and vagal nerve dysfunction as possible mechanisms in the pathophysiology of adult CVS.

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NEURO-MUSCULAR EVALUATION IS AN IMPORTANT COMPONENT IN EVALUATION OF PATIENTS WITH GASTROPARESIS

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Purpose of Study: Patients with Gastroparesis (GP) are often described as having neuro muscular disease. However, little quantification of systemic Neuro-muscular diseases has been performed. We reported data on 46 GP who underwent thorough Neuro muscular evaluation: 91% were women, mean age recorded for all patients was 40 yrs. 93% were Caucasians and 7% were African Americans with etiology of 78% idiopathic, 12% diabetic and 10% post-surgical.

Methods Used: Gastroparesis assessment was done by symptom evaluation for nausea, vomiting, bloating, abdominal pain and total symptom score in addition to Gastric emptying studies (GET) and electrogastrogram (EGG) studies. Neuronal evaluations for Motor and sensory components of limbs was done by Electromyogram (EMG) nerve conduction studies. Specific neuronal antibody and genetic screening was performed on our patient with gastroparesis who also presented with some neuro-muscular symptoms. ELISA, western blot recombinant and indirect immunofluorescence screenings were used to detect anti-neuronal nuclear autoantibody (ANNA) types 1, 2, and 3; purkinje-cell cytoplasmic autoantibodies (PCA) type 1, 2 and voltage-gated potassium channels (VGKC). Genetic markers for Thymidine phosphorylase (Tp), a mitochondrial gene mutation was also done in this population.

Summary of Results: See table.

Conclusions: Evaluation of gastroparetic patients with Neuro-muscular diseases shows a variety of abnormalities. The findings here could help further our understanding of the pathophysiology of gastroparesis at receptor level involving the neuronal component.

Table for Results

PARAMETERS	NUMBER OF PATIENTS ASSESSED	% ABNORMAL DETECTED
Plasma amino acid	22	36%
Plasma lactic acid	25	8%
Anti-nuclear antibodies(ANA)Western blot	24	25%
Striated muscle antibody	17	12%
ANNA-1,2,3	23	10%
p/q Type calcium channel antibody	23	4%
Anti-acetylcholine receptor ganglionic antibody	23	4%
v-g Neuronal potassium channel antibody	19	11%
Lower limb sensory	21	33%
Lower limb motor	21	10%
MNGIE	7	14%

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NEONATAL HEMOCHROMATOSIS: A RARE AND POTENTIALLY FATAL CAUSE OF NEONATAL LIVER FAILURE

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Case Report: Background: Neonatal hemochromatosis (NH) is a rare disease of fetal onset in which excess iron deposition occurs in the liver and non-reticuloendothelial organs such that patients present with liver failure in

the neonatal period. The prognosis has historically been poor. Aim: To raise awareness of this potentially lethal disease that, when diagnosed and treated early, may lead to improved outcome. Case report: A 36-week gestation Caucasian female infant was born via vaginal delivery with meconium staining at a birth weight of 1976 grams. The baby was jaundiced with hepatosplenomegaly and diffuse petechiae at birth. Laboratory tests after birth revealed t. bili 18.5, d. bili 13.6, AST 859, ALT 247, alk phos 152, albumin 1.4, glucose 50, H/H 15/42.8, platelets 27,000, PT 30.6, and INR 2.81. The t/d bili peaked at 36.9/24.3 on day of life 2. Infection was excluded by extensive testing. A ferritin level on day of life 9 was 11,571 ng/mL. An MRI of the abdomen was inconclusive for diagnosis. An oral mucosal biopsy revealed iron in the minor salivary glands. The patient was initially treated with antibiotics, AquADEK vitamins, Actigall, platelet transfusions, and fresh frozen plasma. After the diagnosis was made, the patient received 2 doses of IVIG and was placed on selenium and N-acetylcysteine. The patient's coagulopathy improved, the platelet count increased, and the hyperbilirubinemia decreased. The neonate is currently stable on full feeds in the NICU. Discussion: Since NH is rare, it may be missed if not included in the differential diagnosis. If the diagnosis is not made early, the treatment may not be effective and the patient may require liver transplantation. Recent evidence (J Pediatr 2009;155 (4):566) suggests that the etiology may be related to maternal alloimmunity directed at the fetal liver with improved outcome after treatment with IVIG and exchange transfusion.

Health Care Research

Concurrent Session

1:00 PM

Saturday, February 27, 2010

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IDENTIFYING PEDIATRIC ASTHMA PATIENTS WHO DON'T RECEIVE RECOMMENDED CARE PRIOR TO HOSPITAL DISCHARGE

AE. Lintzenich, R. Teufel, W. Basco *MUSC, Charleston, SC.*

Purpose of Study: Recommended care prior to discharge from an asthma hospitalization includes prescribing controller medications, providing asthma education, and scheduling a follow-up appointment. Our objective was to identify factors associated with receipt of recommended discharge care in a population of hospitalized children with asthma.

Methods Used: Retrospective chart review of patients 2-18 years with primary diagnosis of asthma admitted to MUSC Children's Hospital in 2005. Demographic variables examined were: gender, race, age (2-6 yrs v. 7-18 yrs), primary payer (commercial v. Medicaid/other), and season of admission (April-September v. October-March). We included 3 measures of severity: ICU admission, desaturation, and length of stay. Recommended discharge care variables were: prescription for inhaled corticosteroids (ICS), asthma education, and scheduling a follow-up appointment. All variables were categorical and bivariate analyses utilized chi-square tests. Logistic regression models identified patient and clinical variables associated with receipt of recommended care prior to discharge.

Summary of Results: 123 subjects were analyzed. 58% of subjects were male, 70% black/other, 65% 2-6 years old, 75% Medicaid /other, and 67% were admitted between Oct-March. For recommended discharge care: 75% were prescribed ICS, 68% got asthma education, and 66% had a follow-up appointment scheduled. Bivariate analyses showed that 2-6 year olds were less likely to get ICS (67% v. 88% p<.01) and asthma education (62% v. 80% p<.05). Whites and patients admitted Oct-March were less likely to get asthma education (both p<.05). Commercial payer patients were less likely to have follow-up appointments scheduled (p<.05). Multivariable analyses demonstrated that younger children are marginally less likely to get ICS (OR= 0.334 95% CI 0.109-1.020), younger children are less likely to get asthma education (OR= 0.365 95% CI 0.135-0.990) and commercial payer patients are less likely to get follow-up appointments scheduled (OR=0.400 95% CI .168-.953) (all model p<.05).

Conclusions: Younger asthmatics appear less likely to receive inhaled steroids and asthma education at our hospital. Targeting younger patients may be a way to significantly improve delivery of recommended asthma care prior to discharge.

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EMERGENCY DEPARTMENT CARE IN EVALUATION OF NURSING HOME PATIENTS

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Purpose of Study: Emergency Departments (ED) are typically the major providers of acute care for nursing home (NH) residents. Considering that there are more than 1.5 million residents in NH nationally, the cost implications are enormous. The aim was to determine trends in NH patients presenting to the ED.

Methods Used: Data on all NH patients seen in the ED from 7/2007 to 6/2009 was analyzed. All information related to their stay in ED, including presenting complaint, admission/discharge diagnosis, length of stay in ED and overall costs were obtained.

Summary of Results: 490 NH residents were evaluated in the ED over 24 months. 320 were admitted after ED evaluation. 35% of NH residents presenting to the ED were discharged back after evaluation. Of note patients with higher than average discharge rate were those with musculoskeletal/dermatologic, neurologic/psychiatric, and endocrine complaints with 67%, 44%, and 38% discharge rates respectively. On the other hand, patients with lower than the average discharge rate (and higher admission rates) were those with hematologic/oncologic, cardiovascular and renal complaints with 25%, 24%, and 20% discharge rates respectively. Of the total patients finally admitted, 14% were admitted to an ICU. Interestingly, 42% of those presenting with pulmonary complaints and 25% of those with hematologic/oncologic complaints were admitted to ICU as opposed to only 14% of those with cardiovascular complaints. The average time spent in the ED was 11 hours and 30 minutes.

Conclusions: The aim of this study was to see if there were any noticeable trends in patients presenting to the ED from NH. The goal is to develop an understanding of the common acute illnesses and presentations of NH residents who need inpatient hospital care. It is clear that patients who have certain diagnosis/presenting complaints are more likely to get admitted than others and generally the diagnosis correlates with where they get admitted as well. Waiting for test results to exclude lower likelihood illnesses, leads to more time spent in the ED, higher costs, and more patient/family distress. Subsequent focus will be on prospectively studying a large number of NH patients transferred to the ED with the goal of developing a clinical tool that could aid in the triage of sick patients at NH.

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EVALUATING POTENTIAL HEALTH DISPARITIES FOR PEDIATRIC DRUG SUBSTITUTION ERRORS

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Purpose of Study: Because children residing in Health Professions Shortage Areas (HPSAs) experience many health disparities, we evaluated whether HPSA resident children are more likely to experience Look-Alike, Sound-Alike (LASA) drug substitution errors.

Methods Used: Review of 2000-2006 So. Carolina Medicaid data. We previously reported frequencies of LASA errors for 11 LASA drug pairs. For this study, we examined two drug pairs where > 300 subjects received both drugs in the pair (Adderall/Inderal and Prilosec/Prozac) to determine if HPSA residents were more likely to experience an error. We compared subjects who received both drugs AND experienced a LASA error to subjects who received both drugs with no error. Bivariate analyses compared the groups by gender, race/ethnicity, age, year of prescription, and whether they resided in a HPSA (entire county was HPSA). We completed regression models to predict experiencing a LASA error, with HPSA residence as the criterion variable, controlling for the other variables.

Summary of Results: Three hundred thirty-three subjects < 21 years old received both Adderall and Inderal, and 20 (6%) of these experienced LASA errors. Among the 325 subjects who received both Prilosec and Prozac, 15 (4.6%) experienced LASA errors. In bivariate analyses, subjects residing in HPSAs were not more likely to experience a LASA error than subjects not residing in a HPSA: 8.3% of those who experienced an Adderall/Inderal LASA error resided in a HPSA vs 5.8% of Adderall/Inderal subjects experiencing no error ($p > 0.50$). In a similar fashion, 13.3% of Prilosec/

Prozac subjects who experienced a LASA error resided in a HPSA vs 13.9% of Prilosec/Prozac subjects experiencing no error ($p > 0.90$). Male subjects who received both Adderall and Inderal were more likely to experience a LASA error, and this relationship was significant after controlling for other factors in regression analyses (OR 4.7, 95% CI 1.06 - 20.65). Among subjects receiving Prilosec and Prozac, no variable was associated with receipt of a LASA error in either bivariate or multivariate analyses.

Conclusions: Children living in rural areas of this state did not experience disparate frequencies of Look-Alike, Sound-Alike drug substitution errors of the two drug pairs tested. Male subjects receiving Adderall or Inderal may be more likely to experience LASA errors.

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MAMMOGRAPHY AND COLORECTAL CANCER SCREENING: FQHC PATIENTS' KNOWLEDGE, ATTITUDE AND BEHAVIOR

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Purpose of Study: To determine more effective strategies to increase initial and repeat breast and CRC screening, we are conducting a randomized control trial in 6 FQHCs in North LA. This updated report is on baseline data on the knowledge, attitudes and behavior (KAB).

Methods Used: Eligible patients (women ≥ 40 who had not received a mammogram in the last 2 years; men and women ≥ 50 over who were not up-to-date with CRC screening) were given a structured interview that assessed literacy and breast cancer and CRC screening KAB.

Summary of Results: Of the 718 patients enrolled in the mammography study to date, 66% are AA, 34% white; 42% are reading < 8th grade level. 82% reported they had received a recommendation for mammography from a doctor. 76% had previously had a mammogram, yet 43% of these had not been rescreened in 4 or more years. Attitudes about mammograms were positive: 93% believed if breast cancer is detected early their chances of survival are good to very good. The most common misconception about mammograms was the age of initial screening - 71% believed it was < age 40. Of the 596 patients enrolled in the CRC study to date, 67% are AA, 33% white; 43% are reading < 8th grade level. 23% reported they had completed a FOBT before, but 54% had not completed another FOBT > 3 years. Only 36% reported their doctor recommended CRC screening. The most common reasons patients reported not being tested was they put it off (23%), did not know it was needed (30%). Awareness of CRC was high but knowledge was low: 96% said they had heard of CRC but 24% of these could not say what it was. Attitudes about CRC screening were positive. 90% believed if CRC is found early that their chances of survival were good to very good. The most common misconception about CRC screening was the age a person should start getting screened - 66% believed it was < 50 years old.

Conclusions: In women cared for in FQHCs, lack of knowledge about breast cancer screening is not a barrier. The majority had had an initial mammogram and most had received a recommendation from their doctor. However, these women were not up-to-date with their screening. Eligible patients cared for in FQHCs have a high awareness of CRC but few have been screened or offered screening.

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COMPARISON OF MEDICAL LITERATURE SEARCHES USING EITHER PUBMED CENTRAL OR GOOGLE SCHOLAR

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Purpose of Study: Medical literature searches provide critical information both for clinicians and for researchers (including residents). Given the ongoing development of new search engines, the best search strategy for identifying relevant literature reporting the most current, high quality research is unclear.

Methods Used: The authors used PubMed Central and Google Scholar to identify literature relevant to four clinical questions of varying topics. Abstracts from the first twenty citations for each search were reviewed and classified into three categories (relevant, possibly relevant, and not relevant). The agreement between reviewers was measured using the Kappa statistic;

the agreement between search engines was calculated using percentage overlap. We also used descriptive statistics and t-tests to compare the search engines by their articles' total number of citations and the corresponding journals' impact factor.

Summary of Results: Reviewers ranked 57 - 100% of the PubMed articles and 38-100% of the Google Scholar articles as at least partially relevant. There was good agreement between the reviewers on abstract classification (Kappa: 0.35 to 1.0; all p-values <0.05). The number of overlapping articles ranged from 0 to 9. On three questions, the articles recovered by Google Scholar had higher median number of citations ($p < 0.05$); on one question, the articles recovered by Google Scholar had a higher median journal impact factor ($p < 0.05$).

Conclusions: Searches using PubMed Central and Google Scholar can give substantially different results. Assuming that both search the same body of literature, the small number of articles ranked by both in the top 20 indicates potentially very different relevance ranking algorithms. Reviewers more often assigned higher relevance to articles found by Google Scholar. Articles identified by Google Scholar have a higher median number of citations and may have higher journal impact factors. These results likely reflect characteristics highly ranked by the Google Scholar search algorithm, but the identification of frequently cited articles probably has value for initial searches.

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ADHERENCE TO DEMENTIA GUIDELINES IN THE TEXAS PANHANDLE

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Purpose of Study: Dementia is the leading cause of disability among older adults. Alzheimer's disease (AD) comprises 55% to 77% of all dementia diagnoses. Studies show that dementia is the most significant risk factor for institutionalization and currently more than 1.5 million Americans reside in nursing homes. This number is expected to more than triple by the year 2030. The Alzheimer's Association developed the Best Practices of Dementia Care Guidelines in 2006 for nursing homes and they have been adopted by the U.S. Department of Health and Human Services. This study was designed to assess the adherence rate of Texas Panhandle nursing homes to these current guidelines and to identify opportunities for improvement.

Methods Used: Surveys were sent to all 34 nursing homes in the Texas Panhandle that were officially listed. The online survey had 44 questions presented in a multiple-choice format and were analyzed using Microsoft Excel.

Summary of Results: 20 of 34 (59%) nursing homes had administrators or MDS Coordinators complete the survey. Nursing homes reported an average of 45 (range 2-100) residents with the diagnosis of dementia. Responses to key questions about "Best Practices of Dementia Care" included: 1) screening for dementia and depression upon admission to the facility: 50% (goal 100% for all); 2) of those that do screen, only 32% repeat screening after a significant behavior change is noted; 3) close monitoring of residents on some type of mood stabilizing agent or antipsychotic medication: 45%; 4) training of staff about falls and pressure ulcers: 100%; 5) advance care planning: 100%; 6) recreational activities for residents: 100%; 7) knowledge of local support groups for families 41%; 8) willing to have staff attend in-service training every 1-3 months: 72%.

Conclusions: This study suggests that while certain aspects of the "Best Practices" are being employed by area nursing homes, there remain some important deficiencies. Fortunately, the survey shows great openness on the part of the majority of nursing homes towards learning more about the guidelines and improving care for this growing population of residents with dementia. Educational activities should be provided as soon as is feasible for these interested facilities.

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BLOOD CULTURE CONTAMINATION RATE INCREASES IN TIMES OF EMERGENCY DEPARTMENT CROWDING

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Purpose of Study: Emergency department crowding (EDC) is an increasingly serious problem. EDC has been shown to be associated with

poor patient and staff satisfaction and inferior outcomes. Blood cultures are commonly performed in a pediatric emergency department and contamination of those cultures sometimes occurs. Contamination of blood cultures results in subsequent unnecessary testing, with accompanying cost - an undesirable outcome. The purpose of this study was to determine if blood culture contamination is more common during times of EDC.

Methods Used: A search of the computerized database of Arkansas Children's Hospital was performed to identify all patients who had a blood culture submitted from the pediatric emergency department (ED) between January and March 2008. The chart of each patient was reviewed to identify the patient demographic data and the identification of any organism on the blood culture. The organism was defined as either pathogen or contaminant by a physician chart reviewer. The emergency department computerized tracking board was queried to determine ED occupancy at the time the culture was drawn. EDC was defined as either 20% or 50% overcapacity. Chi square was used to compare groups. The study was reviewed and approved by the UAMS IRB.

Summary of Results: There were 1440 cultures performed on 1408 patients in the study period. When the ED occupancy was less than 20% overcapacity, 575 cultures were drawn with a 3.13% contamination rate. When the ED occupancy was over 20% overcapacity, there were 862 cultures drawn with a contamination rate of 5.34% ($p < 0.047$). When the ED was less than 50% overcapacity, there were 914 cultures performed with a contamination rate of 3.83%. When the ED was greater than 50% overcapacity, there were 525 cultures performed with a contamination rate of 6.10% ($p < 0.049$).

Conclusions: Blood culture contamination rates are higher when the emergency department is crowded. Crowding may cause the staff to hurry and be less meticulous in their antiseptic technique. Increased blood culture contamination is another undesirable outcome associated with emergency department crowding.

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ACCESS TO HEALTH SERVICES AND ADHERENCE TO ANTIHYPERTENSIVE MEDICATIONS AMONG OLDER ADULTS

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Purpose of Study: Access to health services may be an important determinant of medication taking behavior in older adults. We examined the association of patients' satisfaction with the availability of pharmacy services and the convenience of their doctor's office location with adherence to prescribed antihypertensive medications.

Methods Used: Data were analyzed from the baseline survey of the Cohort Study of Medication adherence among Older adults (CoSMO), a study conducted among adults ≥ 65 years old who were enrolled in a managed care organization and treated for hypertension ($n=2194$). Participants were asked to rate their satisfaction with the availability of pharmacies and the convenience of their doctor's office location using questions from the Group Health Association of America (GHAA) satisfaction survey. Dissatisfaction with access to these services was defined as answering "poor" or "fair" on the GHAA questions. Adherence to antihypertensive medication was assessed with the eight-item Morisky Medication Adherence Scale (MMAS-8); suboptimal (low or medium) medication adherence was defined as MMAS-8 scores < 8 .

Summary of Results: The mean age of participants was 75.0 ± 5.6 years, 30.5% were black, 58.5% were women, 48.4% had suboptimal levels of antihypertensive medication adherence, 6.7% reported they were dissatisfied with the availability of pharmacy services, and 9.5% reported they were dissatisfied with the convenience of their doctor's office location. Compared to participants who were satisfied, those who were dissatisfied with the availability of pharmacy services were 1.28 (95% CI 1.05, 1.57) times more likely to have suboptimal medication adherence, and participants who were dissatisfied with the convenience of their doctor's office location were 1.27 (95% CI 1.07, 1.49) times more likely to have suboptimal medication adherence.

Conclusions: In the current study, participants who were dissatisfied with the availability of pharmacy services and the convenience of their doctor's office location had lower adherence to prescribed antihypertensive medications.

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CHILD WELFARE CASEWORKER AND RESOURCE PARENT TRAINING: OPPORTUNITIES FOR TECHNOLOGY TO ENHANCE ACCESS AND QUALITY OF TRAINING

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University of Oklahoma College of Medicine, Oklahoma City, OK.

Purpose of Study: The purpose of this study was to describe Resource Parent and Case Worker awareness and openness to various web-based methods of receiving training about health care issues related to foster children.

Methods Used: Case workers (CW) and Resource Parents (RP) throughout Oklahoma were invited to complete online surveys assessing knowledge of and openness to web-based training methods. CW and RP surveys were separate, but comparable in content. Survey content was developed through focus groups held with CW and RP and discussions among a collaborative panel of stakeholders. Training methods assessed included live and non-live webseminar, interactive chat, video broadcasting, and podcast services. Descriptive analysis of the survey data was conducted. Missing data and "Not Applicable" responses were excluded from analysis.

Summary of Results: Six hundred CW (56% of those invited) and 320 RP (28% of those invited) completed the survey from July - August 2008. The sample included CW from 84% of Oklahoma counties and RP from 68% of counties. Across the various technologies, over 80% of CW expressed knowledge of each of the methods, with the exception of podcast (55.1%). High percentages of CW expressed willingness to use web-based technologies, ranging from 79.6% (podcast) to 90.1% (live web seminar). Similar to CW, over 80% of RP expressed knowledge for each of the methods except podcast (60.8%), with a majority of RP reporting a willingness to use various technologies ranging from 72.4% (podcast) to 90.4% (video broadcasting). A higher percentage of RP reported currently receiving training through an online RP college (77.3%) compared to more traditional training method, such as OKDHS conferences and seminars (46%).

Conclusions: The findings from this study strongly support the potential for effective implementation of web-based methods of training for CW and RP. The majority of both CW and RP express knowledge of these technologies, and though prior experience was not assessed, it is likely that many CW and RP have used these technologies. The high rate of openness to web-based technologies supports utilization of these methods in OK child welfare and indicates that the change should be well accepted.

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THE MERCI RETRIEVER DEVICE AS A TREATMENT FOR ACUTE ISCHEMIC STROKE: THE LADY OF THE LAKE HOSPITAL (BATON ROUGE) EXPERIENCE

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Purpose of Study: Acute ischemic stroke is a common and devastating disease that accounts for 160,000 mortalities a year in the United States and is associated with long-term disability. Treatment options for acute ischemic stroke have advanced to include not only pharmacological but also mechanical therapies. Several mechanical techniques are available for clot removal or lysis. They consist of angioplasty, microsnare, use of lasers, ultrasonography, and the MERCI Retriever Device which can physically grab and remove the thrombus endovascularly. Although indications for pharmacologic thrombolytic agents are generally limited to the first 3 to 6 hours after the onset of the symptoms, MERCI Retriever device has been successfully used to manage acute stroke patients up to 8 hours after the stroke occurred.

Methods Used: Eight patients presented with signs and symptoms of ischemic strokes with symptoms of greater than 6 hours duration. MERCI devices were used to try to reestablish blood flow in the occluded vessels (4 left medial cerebral arteries, 3 right medial cerebral arteries, and 1 basilar artery).

Summary of Results: The X5 and X6 MERCI devices were used in these cases with a success rate of 50% (4/8). In one case, balloon angioplasty markedly improved blood flow after failed attempts with the MERCI device. The number of attempts ranged from 1 to 6 with a mean of 4.8. Among the 7 patients who survived the procedure, two patients returned to pre-stroke baseline function and 5 patients survived with residual functional deficits caused by the ischemic stroke. Life support was withdrawn from one patient after unsuccessful recanalization of the basilar artery.

Conclusions: MERCI retriever is a new device which provides a high-success-rate alternative treatment for ischemic strokes that pass the traditional 6-hour clinical window for pharmacological thrombolysis.

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ASSOCIATION OF HEALTH LITERACY AND DIABETES SELF-CARE UTILIZING THE INFORMATION-MOTIVATION-BEHAVORAL SKILLS MODEL

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Purpose of Study: Limited health literacy has been recognized as an important public health issue and barrier to managing chronic illnesses. To date, results have been mixed about whether health literacy is a barrier to managing diabetes and, in turn, achieving glycemic control. Secondly, the mechanisms underlying the relationship between health literacy and outcomes in diabetes are unknown. Thus, we performed path analyses to assess health literacy as a direct predictor of diabetes self-care behaviors and glycemic control, and applied the Information-Motivation-Behavioral Skills (IMB) model constructs in the predicted pathway to test whether health literacy is indirectly related to diabetes self-care and glycemic control through the IMB elements.

Methods Used: Patients with diabetes were recruited from an outpatient primary care clinic. Information gathered pertained to demographics, health literacy (REALM-R), diabetes knowledge (information), diabetes fatalism (personal motivation), social support (social motivation), and diabetes self-care (behavior). Hemoglobin A1C values were extracted from patients' medical records. Structural equation models tested the predicted pathways in our estimated models.

Summary of Results: Health literacy was indirectly related to self-care behaviors through relations with social motivation ($r = -0.20$, $p < 0.05$). No direct relationship was observed between health literacy and self-care behaviors or A1C. More diabetes knowledge ($r = 0.22$, $p < 0.05$), less fatalistic attitudes ($r = -0.22$, $p < 0.05$), and more social support ($r = 0.27$, $p < 0.01$) were independent, direct predictors of diabetes self-care behavior; and through behavior, were related to glycemic control ($r = -.020$, $p < 0.05$).

Conclusions: Health literacy was only indirectly related to behavior through social motivation. Consistent with the IMB model, having more information (more diabetes knowledge), personal motivation (less fatalistic attitudes), and social motivation (more social support) was associated with behavior; and behavior was the sole predictor of glycemic control. Our findings indicate that for patients with lower health literacy, enhancing social motivation in diabetes education programs would result in more effective self care behaviors and improved glycemic control.

**Hematology and Oncology II
Concurrent Session**

1:00 PM

Saturday, February 27, 2010

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EFFECT OF PROTEIN KINASE C β SPECIFIC INHIBITION ON ACUTE LYMPHOBLASTIC LEUKEMIA CELL LINES

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Purpose of Study: Acute lymphoblastic leukemia (ALL) is the most common leukemia in children and accounts for 20% of acute leukemia in adults. The intensive induction-consolidation-maintenance therapeutic regimens used currently have improved the 5-year disease free survival to around 80% in children and to 25%-40% in adults. In the present era of target-specific therapy, PKC β targeting arose as a new, promising, and well tolerated treatment strategy in a variety of neoplasms, especially in B-cell malignancies. PKC β plays a major role in B-cell receptor signaling, but studies describing the role of PKC β in B-cell ALL are lacking. In the present study, we measured the sensitivity of a variety of B-cell ALL cell lines to PKC β specific inhibition.

Methods Used: Three cell lines were studied: RS4;11 (characterized by the t(4;11) chromosomal abnormality), TOM-1 (characterized by the t(9;22) chromosomal abnormality), and REH (characterized by the t(12;21)

chromosomal abnormality). Cells were tested for PKC β 1 and PKC β 2 expression by immunoblot. Cell viability was measured when PKC β -specific inhibitor at concentrations of 1, 2.5, 5, 10, 20 and 30 μ M was added for 48 hours in the presence of 10% fetal bovine serum (FBS). MTS assay was performed to quantify cell viability.

Summary of Results: Results showed that all three cell lines express PKC β 1 and PKC β 2. Treatment with PKC β -specific inhibitor resulted in a dose-dependent inhibition of cell proliferation; Sensitivity was evident at 1 μ M for RS4;11 cell line, and at 2.5 μ M for TOM-1 and REH cell lines, with 10% cell growth inhibition; Growth inhibition increased to 90% for all cell lines at an inhibitor concentration of 30 μ M.

Conclusions: These results indicate that PKC β plays an important role in the malignant process in B-cell ALL, and suggest that PKC β targeting should be considered as a potential treatment, whether in combination with the current regimens used or as a single agent monotherapy. Ongoing studies in our lab will detail the mechanism of PKC β inhibition and uncover possible relationships between PKC β and adverse cytogenetics like t(4;11) and t(9;22).

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PROFOUND VITAMIN D DEFICIENCY IN ADOLESCENTS WITH SICKLE CELL CHRONIC PAIN

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Purpose of Study: Vitamin D deficiency (VDD) is extremely common among African Americans. Over 40% of blacks have severe VDD (25 hydroxyvitamin D (25(OH)D) <15ng/mL. Poor vitamin D status causes increased fracture risk, myopathy & chronic bone pain. The Mayo Clinic recently reported a high prevalence of severe VDD in patients with persistent, nonspecific musculoskeletal pain & recommend routine screening for VDD in these patients. Sickle cell disease (SCD) affects primarily AA and about 10% of children & adolescents with SCD have daily debilitating pain. Vitamin D deficiency is seen in 64–100% of persons with SCD depending on the season. The relationship between vitamin D status & SCD chronic pain has not been investigated. We propose that SCD chronic pain is associated with severe VDD.

Methods Used: Sixteen African American adolescents with SCD attending the Sickle Cell Chronic Pain Clinic at Children's Healthcare of Atlanta were screened for VDD over an 18 month period. Dual x-ray absorptiometry scans (DEXA) were obtained on 11 subjects. Multidisciplinary management of chronic pain included optimizing sickle cell management using the fetal hemoglobin modifier Hydroxyurea (HU), adjuvants, physical therapy and intensive psychotherapy.

Summary of Results: Of the 16 subjects evaluated, median age was 16y (range 10-19y); 75% were female. Genotype distribution was: HgbSS(n=13); HgbSC(n=2); HgbSB+Thal(n=1). Fourteen subjects (87.5%) were on HU. The mean 25(OH)D was 8.81 $\pm$ 3.25 ng/mL (range <5-15ng/mL). All but one subject was profoundly vitamin D deficient (25(OH)D <15ng/mL). Eleven subjects had DEXA scans; 54% met criteria for osteopenia (whole body (WB) z score <-1.5). The 2 subjects (18%) with undetectable 25(OH)D <5ng/mL met criteria for osteoporosis (WB z score <-4.3 and <-3.9 respectively). Having a low vitamin D level was not predictive for abnormal bone density (chi-square 1.2953, p= 0.2551).

Conclusions: Profound VDD is common in adolescents with SCD chronic pain and should be considered in differential. Having undetectable 25OHD levels was associated with severe abnormalities in bone density. We have initiated a prospective longitudinal study of VDD in SCD as well as a randomized controlled trial to determine the efficacy of vitamin D replacement in SCD chronic pain.

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FACTORS INFLUENCING RE-EXCISION RATES IN BREAST CONSERVING SURGERY FOR CANCER

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Purpose of Study: Breast conserving surgery (BCS) requires complete excision of the tumor with negative surrounding margins. Current comprehensive pathologic analysis carefully evaluates all margins, and 30-50% rates of surgical re-excision to obtain adequate margins have been reported. Various techniques, including alternatives to wire-localization,

intra-operative margin assessment, & specimen mammograms have reported mixed success in reducing re-excisions, however, these typically require new equipment & may increase operative time. Cavity shave margin (CSM) removal is a simple surgical technique that utilizes existing equipment to potentially reduce re-excisions. This study evaluates the role of this technique in reducing re-excisions.

Methods Used: Single institution retrospective review identified 522 breast cancers treated with BCS between 2005-2009. Patients underwent either standard partial mastectomy (SPM) with additional margins taken at the discretion of the surgeon, or CSM. Data collected included demographics, pathology, neoadjuvant chemotherapy, surgeon, need for re-excision, & final surgery.

Summary of Results: 455 patients underwent SPM & 67 underwent CSM. Analysis between the groups revealed no statistically significant differences in tumor pathology/size, patient age, localization technique, residual tumor removed, extensive intra-ductal component, or neoadjuvant chemotherapy. Overall re-excision rate was 43%. The most common reason for re-excision was the presence of DCIS at a margin. The SPM group underwent 213 re-excisions (46.8%), while only 16/67 (23.9%) in the CSM group required reoperation for margin clearance (p=0.0003). Analysis of the pathology results from the SPM only group requiring re-excision revealed that 143/213 (67.1%) patients could have been spared the 2nd operation if CSM was performed at the initial surgery. The only other statistically significant difference between the two groups was the performance of total mastectomy as the definitive procedure, with more patients in the SPM group choosing this as their final treatment (p=0.009), even though these patients were not more likely to have residual tumor.

Conclusions: This study supports the use of CSM as an accessible & easily implemented technique that significantly reduces re-excision rates & rates of total mastectomy.

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NOSOCOMIAL INFECTION RATES AMONG PEDIATRIC ONCOLOGY PATIENTS: A RETROSPECTIVE STUDY EXAMINING THE EFFICACY OF HIBICLENS®

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Purpose of Study: Hematopoietic stem cell transplant (HSCT) patients are at the highest risk for nosocomial infections (NI) among oncology patients. Therefore, routine daily bathing with the antimicrobial antiseptic Hibiclens® is often integrated as standard of care for these patients. This study examined the rate of NI among HSCT pediatric oncology patients as compared to the general pediatric oncology population to evaluate the efficacy of Hibiclens® as a prophylactic agent.

Methods Used: This retrospective study examined all pediatric oncology inpatients over an eighteen month period at Children's Hospital in New Orleans, LA. Patients were classified into two groups: the non-transplant oncology (control) group and the HSCT (study) group. NI was defined as the presence of fever (temperature >38°C) >24 hours after admission, and/or presence of positive cultures obtained from blood, urine, or stool samples. Culture-confirmed infections were termed hospital-acquired infections (HAI). Febrile patients without culture confirmation were classified as nosocomial fever of unknown origin (nFUO). Infection rates were calculated as the incidence density (ID) for each group (# occurrences/100 days).

Summary of Results: Fifteen patients were eligible for the HSCT group, and four hundred and forty-five for the study group. The overall infection ID in the control group was 1.98, and 1.10 in the study group (P=0.20). Within the sub-categories, the ID of nFUO and HAI was 0.89 and 1.10 in the control group, and 0.44 and 0.66 in the study group, respectively (P=0.63, 0.21). Further data analysis was calculated utilizing the Kaplan-Meier survival curve (P=0.09).

Conclusions: Hibiclens® bathing appears to decrease the NI ID among HSCT oncology patients compared to the non-transplant population, though not a statistically significant difference (P > 0.05). It can be reasonably inferred that these findings fall short of statistical relevance due to the group size discrepancy, dictated by the small amount of HSCTs performed annually. Additional research is required to further examine these findings, and to examine implementing routine Hibiclens® washing as the standard of care among all oncology inpatients.

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SELECTIVE PROTEIN KINASE C β INHIBITION INDUCES APOPTOSIS AND ARRESTS CELL CYCLE IN AIDS-RELATED NON-HODGKIN LYMPHOMA CELL LINES

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Purpose of Study: AIDS-related Non-Hodgkin Lymphoma (AIDS-NHL) constitutes an aggressive variety of lymphomas. In the present era of target-specific therapy, PKC β targeting showed promising results in preclinical and clinical studies involving a wide variety of cancers. Studies describing the role of PKC β in AIDS-NHL are primitive if not lacking.

Methods Used: Three cell lines were studied: 2F7 (AIDS-Burkitt's Lymphoma), BCBL-1 (AIDS-Primary Effusion Lymphoma) and UMCL01-101 (AIDS-Diffuse Large B Cell Lymphoma). Cells were tested for PKC β 1 and PKC β 2 expression by immunoblot. Cell viability was measured in the presence of a PKC β -specific inhibitor at concentrations of 5, 10, 20 and 30 μ M for 48 hours, the IC50 at 48 hours was determined and used to treat the cells for 24 and 72 hours. MTS assay was performed to quantify cell viability, and TUNEL assay with propidium iodide staining was used to detect apoptotic induction and effect on cell cycle.

Summary of Results: Results showed that 2F7 and UMCL01-101 cell lines express PKC β 1 and PKC β 2, while BCBL-1 expresses only PKC β 1. 2F7 and BCBL-1 were sensitive to PKC β inhibitor with IC50 of 14 and 15 μ M of inhibitor, respectively. UMCL01-101 showed relative resistance to PKC β inhibition with an IC50 of 28 μ M. Incubation in the presence of the correspondent IC50 induced significant apoptosis in all cell lines starting after 2 hours of treatment; UMCL01-101 cell line was not significantly affected when incubated in the presence of 14 μ M. Our results also showed cell cycle inhibition in 2F7 and BCBL-1 starting respectively after 2 and 8 hours of incubation with the correspondent IC50; UMCL01-101 showed no features of cell cycle inhibition at high concentration (IC50) or low concentration (14 μ M) of the inhibitor. BCBL-1 cell line findings implicate PKC β 1 as a regulator in these cells.

Conclusions: PKC β plays an important role in AIDS-related NHL survival, and suggest that PKC β targeting should be considered in a broader spectrum of NHL. Ongoing studies will detail the mechanism of PKC β inhibition and uncover the underlying mechanism of resistance in PKC β expressing UMCL01-101 cells. This mechanism may be considered for exclusion from treatment.

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INTERFERON- α AUGMENTS REGULATORY T CELL (TREG) DEPLETION TO BOOST ANTI-TUMOR IMMUNITY AND CLINICAL RESPONSE IN OVARIAN CANCER

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Purpose of Study: Tumors elicit immune responses. Nonetheless, immune dysregulation in cancer hinders anti-tumor immunity. We hypothesize that Tregs and dysfunctional dendritic cells (DC) are causes of this immune subversion. We use denileukin difitox (DT) to deplete Tregs and interferon (IFN)- α to improve DC function and activate anti-tumor T cells. This strategy could reduce immune subversion and improve anti-tumor immunity.

Methods Used: C57BL/6 mice were challenged intraperitoneally with syngeneic OVA-expressing ID8 ovarian carcinoma (ID8/OVA) and treated 2 weeks later with DT (5 μ g/week), human hybrid IFN- α (20,000 units 4 days/week), DT+IFN- α , or PBS control. Flow cytometry and in vivo analyses were used to study immunity, which correlated with mouse survival. Tumor (OVA)-specific immunity was tested with an in vivo OVA-specific killing assay and OVA-specific T cells.

Summary of Results: DT boosted survival in tumor-bearing mice compared to PBS. DT+IFN- α boosted survival greater than either drug alone. Treatment effects disappeared in tumor-bearing Rag2-/- mice (lacking T and B cells), suggesting adaptive immunity is required. IFN- α did not reduce Treg numbers or function. IFN- α , DT, or DT+IFN- α increased OVA-specific cytotoxic T lymphocyte (CTL) activity compared to PBS. DC from tumor-draining lymph nodes of untreated mice suppressed T cell proliferation in vitro, but DCs from IFN- α treated mice were not suppressive. IFN- α induced DC CD86 expression in vivo, suggesting that IFN- α matured DC.

We transferred CD8+ OVA-specific T cells (sensitive to IFN- α) into ID8/OVA challenged type I IFN receptor null mice (insensitive to IFN- α). IFN- α elicited significant OVA-specific CTL activity, which was further enhanced by transfer of wildtype DCs. Addition of IFN- α to DT in 2 human patients with refractory epithelial ovarian carcinoma who failed single-agent DT therapy improved immunity and rescued a clinical response.

Conclusions: These data suggest that IFN- α : i) augments the clinical benefit of Treg reduction in mice and humans with ovarian cancer and ii) improves anti-tumor immunity through effects directly on T cells, and indirectly through DC.

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DEVELOPMENT OF A TRANSGENIC IN-VIVO ZEBRAFISH MODEL OF MEDULLARY THYROID CANCER

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Purpose of Study: Medullary Thyroid Cancer (MTC) is a rare and aggressive malignancy of thyroid C cells driven by various mutations in the RET proto-oncogene. Both familial and sporadic forms of MTC frequently metastasize to regional lymph nodes at the time of diagnosis of the primary tumor. Because of this, adjuvant therapy after surgical resection is indicated, but so far, few drugs have shown to be effective. One of the primary hurdles to drug discovery is the difficulty in gathering sufficient number of patients to perform clinical trials with sufficient power. A robust animal model of MTC would aid development of novel targeted therapeutics. Recently, zebrafish have proved to be an ideal vertebrate cancer model because of the similarity of cancer pathogenesis to humans, short reproduction time, genetic tractability, and easy handling of a large number of organisms at a time. Another feature is the utilization of a site-specific recombination-based cloning technique that can more efficiently create transgenic models of zebrafish (Tol2kit). This method allows the creation of molecular constructs with a desired promoter, coding sequence, and 3' element in a Tol2 transposon backbone.

Methods Used: In our work, we use a zebrafish calca promoter upstream of nuclear-localized or membrane-localized mCherry (a monomeric red fluorophore) to facilitate visualization of c-cell development. Following this, our calca promoter is placed upstream of a human RET proto-oncogene sequence containing either C634R or M918T mutations, which predispose to MTC in the MEN2A and MEN2B syndromes respectively.

Summary of Results: By generating a large number of affected zebrafish, we hope to rapidly assess known and novel agents for activity against MTC. In addition, we hope to leverage the power of zebrafish in vivo imaging and genetic screens to gain insight into the development of MTC.

Conclusions: This knowledge will greatly facilitate treatment and management of MTC patients, which has found lackluster success so far.

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CLINICAL OUTCOME OF CHEMORADIOTHERAPY IN ELDERLY VETERANS WITH LOCALLY ADVANCED UNRESECTABLE NON-SMALL CELL LUNG CANCER (NSCLC)

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Purpose of Study: The majority of lung cancer patients are elderly. Data on optimal chemoradiotherapy in the elderly patients is limited. We conducted a retrospective review to compare the outcomes of sequential versus concurrent chemo radiation in the elderly patients with advanced loco-regional lung cancer at Veterans Affairs (VA) hospital.

Methods Used: Medical records of patients with NSCLC treated at the VA Medical Center in Jackson, MS and Milwaukee, WI from January 2000 to December 2007 were abstracted. Patients were included if they were > 65 years old and had received both chemotherapy and thoracic radiotherapy as definitive treatment for clinically staged IIIA and B NSCLC (excluding pleural effusion). Patients who received palliative radiation only were excluded.

Summary of Results: 87 elderly patients with locally advanced NSCLC were included. Sequential chemoradiotherapy was delivered in 26 patients and concurrent in 61 patients. Demographics of the patients receiving sequential

and concurrent chemoradiotherapy respectively are: age 74 and 72 years, all males, African-American race 23% and 20%, Stage IIIB 23% and 36%. Median radiotherapy dose delivered with sequential regimen was 6230Gy versus 6300Gy with the concurrent regimen. Patients receiving sequential chemoradiotherapy received carboplatin and taxane doublet intravenously q 3 weeks; carboplatin -taxane doublet was given weekly in concurrent arm. There was only 1 treatment related death. 12 patients (7 in concurrent and 5 in sequential arm) survived for less than 6 months. Survival among the two groups did not differ statistically. Median survival was 20 months in the sequential arm vs. 17 months in the concurrent arm, p value=0.97.

Conclusions: Sequential chemo radiotherapy may be as effective as concurrent chemoradiotherapy and less toxic in elderly VA patient population and both sequential and concurrent chemoradiotherapy are feasible options in elderly patients with locally advanced lung cancer.

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ESTROGEN NEGATIVE PROGESTERONE POSITIVE BREAST CANCER: PROGNOSIS AND OUTCOME

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Purpose of Study: Breast cancer is the most common cancer in women and the second leading cause of death in the United States. The effect of endocrine therapy has been confirmed in all stages of breast cancer and the responsiveness of a tumor to hormonal therapy is an important parameter in its management. Hormone receptor therapy provides both predictive and prognostic information. The concept that ER receptor predicts the clinical response to hormone therapy in both local and advanced disease has been adopted since many years. Although the loss of PR receptor was correlated with inferior disease-free survival and overall survival, the impact of PR receptor on response is still unclear.

Methods Used: To investigate the topic, the records of 4100 patients diagnosed with breast cancer in our institution between 1998 -2006 were reviewed. These were classified mainly according to stage and hormonal status. Stage IV breast cancer present on diagnosis was excluded. 26 patients were found to have ER-PR+ breast cancer. Their characteristics were studied in details including hormonal and chemotherapeutic agents received in metastasis and disease free survival.

Summary of Results: 38%(10) of the ER-PR+ breast cancer patients were premenopausal, and 62%(16) were postmenopausal. In the premenopausal group, 30%(3) had stage 0 or I on diagnosis, none of which developed metastasis. 70%(7) had stage II or III and 28.5%(2) of them developed lung metastasis. One of these patients received no hormonal therapy and the other received tamoxifen followed by switching to aromatase inhibitors. In the postmenopausal group, 68.7%(11) had stage 0 or I at diagnosis, none of which developed metastasis. 31.3%(5) had stage II or III and 40%(2) of them developed metastasis. Both of them received aromatase inhibitors only. Mean follow up was 5.5 years.

Conclusions: Our study was limited by the small sample size of patients. None of the early breast cancer stages with ER-PR+ developed metastasis and this might suggest that no hormonal therapy might be needed with these earlier stages, while hormonal therapy seems reasonable for higher stages. None of the treatment modalities correlated with better or worse prognosis. New larger studies are needed for further evaluation of the real prognosis and best treatment modality for this type of breast cancer.

Infectious Diseases II Concurrent Session

1:00 PM

Saturday, February 27, 2010

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IMPACT OF CHRONIC INHALED TOBRAMYCIN ON INCIDENCE OF TOBRAMYCIN RESISTANT PSEUDOMONAS AERUGINOSA IN CYSTIC FIBROSIS

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Purpose of Study: *Pseudomonas aeruginosa* (PA) is the most prevalent bacteria that causes pulmonary infection in cystic fibrosis (CF) patients and has been linked to disease-related morbidity. Chronic, alternating monthly

inhaled tobramycin (TOBI) has become a standard treatment and prophylactic measure against PA in CF patients. TOBI has proven to be effective in improving CF patient weight gain (BMI) and lung function (FEV1) during the first two years. However, the development of tobramycin resistant PA due to TOBI has not been well characterized. This study aims to describe the long term impact of alternating monthly TOBI on incidence of tobramycin intermediate and resistant PA and the impact on BMI and FEV1 in CF patients treated at Arkansas Children's Hospital (ACH).

Methods Used: A retrospective chart review was conducted on CF patients at ACH who previously cultured PA and were treated with TOBI. Length of TOBI therapy, total aminoglycoside exposure, PA and other gram negative cultures and their antibiotic susceptibilities, FEV1, and BMI data were collected 1 year prior to first PA through May 2009.

Summary of Results: Sixty-nine CF patients were evaluated. Twenty-one patients cultured tobramycin resistant mucoid or nonmucoid PA after TOBI initiation. Two patients developed tobramycin resistance prior to TOBI initiation. Tobramycin resistance developed in nonmucoid strains as early as 1 year post TOBI while mucoid strains developed resistance after 2 years. Once resistant PA was cultured, both BMI and FEV1 were negatively impacted.

Conclusions: TOBI has been accepted as a standard inhaled therapy to combat PA and has previously shown to improve CF patients FEV1 and BMI, while decreasing hospitalizations. However, beyond the first two years, no significant impact on FEV1 has been shown. In this study, 30% of CF patients developed tobramycin resistance while on TOBI. This leaves limited future treatment options. A correlation was also found with PA resistance and decreasing BMI and FEV1. Further study is needed to assess whether long term TOBI treatment is warranted in patients beyond the first year of PA colonization as development of multi-drug resistance, decline in BMI, and a decrease in FEV1 place an increase risk for morbidity in the CF patient population.

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CANDIDATE AUTOTRANSORTER PROTEINS AS VACCINE TARGETS

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Purpose of Study: To identify highly-conserved surface-expressed molecules that could be targeted in enterotoxigenic *E. coli* (ETEC) vaccine development.

Methods Used: Two members of the autotransporter (AT) family, EatA, and TibA, have been described previously in ETEC strain H10407. AT passenger domains are commonly surface-expressed in Gram-negative bacteria, and therefore represent possible vaccine targets. We searched for AT proteins in ETEC that might be targeted in vaccine development. Using Rapid Annotation Subsystem Technology (RAST) and other bioinformatic approaches we identified two additional AT genes in ETEC H10407 genome that were absent in commensal strains. Passenger domains of all 4 H10407 ATs were cloned, expressed, purified, and immunoblotted with sera from mice infected with H10407 and convalescent sera from children (ICDDR,B Dhaka) with acute ETEC diarrhea.

Summary of Results: Neither preimmune sera from mice or control patient sera recognized recombinant autotransporter passenger (rATp) domains. Conversely, both immune mouse sera and convalescent sera from ETEC-infected patients recognized rATp domains of all 4 autotransporters in H10407.

Conclusions: Immunoreactivity of rATp domains of ETEC suggests that these proteins are expressed during infections and that these molecules could be viable vaccine targets, similar to the pertactin AT of *B. pertussis*, a component of acellular pertussis vaccines. Like pertactin, many autotransporters promote adherence or mucosal colonization. Colonization is an essential step in the molecular pathogenesis of ETEC infections required for effective toxin delivery. Therefore, studies are presently underway to examine the ability of these AT molecules to prevent intestinal colonization in a murine model of ETEC infection. Because homologues of these AT proteins are found in other pathogenic strains of *E. coli* and *Shigella*, these antigens could induce cross-protective immune responses against multiple intestinal pathogens, possible preventing colonization of each.

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MINOR DIFFERENCES IN GENOME CONFER VIRULENCE IN CHLAMYDIA PSITTACI

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Purpose of Study: Little is known regarding virulence factors of the obligate intracellular pathogen *Chlamydia* due to lack of a genetic system. *Chlamydia psittaci*, a category B select agent, is a zoonosis that causes a clinical syndrome in humans called psittacosis, which manifests as pneumonitis and systemic infection. We sought to determine the molecular and immunological basis of the 1000-fold difference in lethal dose of two *C. psittaci* isolates in a murine psittacosis model.

Methods Used: Mice were infected intraperitoneally with clonal isolates of *C. psittaci* 6BC strain derived from two different laboratories. The lethal and non lethal isolates of *Chlamydia psittaci* were fully sequenced using the Illumina Gene analyzer and compared. The in vitro growth was assessed in peritoneal macrophages in the presence or absence of IFN γ . The in vivo growth and immune responses were characterized by flow cytometry and pathology.

Summary of Results: The two isolates differed by the presence or absence of an extra-chromosomal 7.5kb plasmid in the virulent strain and 10 non-synonymous single nucleotide polymorphism (SNP) in the chromosome. The plasmid was cured from the non-virulent strain by serial passage in novobiocin supplemented culture and three new isolates were obtained by limiting dilutions. These three plasmid cured isolates were non-lethal in mice. Lethal and non-lethal isolates disseminated similarly and did not differ in growth kinetics in vitro or in vivo but induced significantly different inflammatory responses. Specifically, non-lethal strains recruited activated macrophages with relatively minor organ damage. Lethal strains caused recruitment of non-activated macrophages and neutrophils that resulted in tissue necrosis. Mice co-infected with the non-lethal isolate survived challenge with the lethal isolate indicating that disease was driven by host inflammatory responses elicited by the virulent strain. Investigation of the individual SNPs is underway.

Conclusions: *Chlamydia psittaci* modulates virulence by alteration of the immune response, which is conferred by small differences in the chromosome.

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INCIDENT CHLAMYDIA TRACHOMATIS INFECTIONS IN HIGH SCHOOLS

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Purpose of Study: To determine the incidence of new infections with *Chlamydia trachomatis* among high school students in an urban US school district.

Methods Used: Between 1995 and 2005, a total of 20,224 high school students were tested for *C. trachomatis* at least once in an annual screening using a commercial nucleic acid amplification test in urine specimens, regardless of sexual activity or symptoms of sexually transmitted diseases (STDs). Of those, 7,950 were screened more than once. The incidence of new infections was calculated among participants with an initial negative test result. Students whose initial test result was positive (n=522) were excluded from analysis. A new infection was estimated to have occurred half-way between the most recent negative test and the following positive test.

Summary of Results: The 3,946 male and the 3,482 female students tested more than once and had an initial negative test result contributed respectively 7,142 and 5,765 person-years of time at risk during which 404 males and 574 females developed a new infection (incidence rates: 5.7 new infections/100 p-yrs for males and 10.0 new infections/100 p-yrs for females. Among students who developed a new infection, the median time between the initial negative test and the following positive test was 10.6 months (11.7 months among males and 9.8 months among females).

Conclusions: There is a high incidence of chlamydia among male and female students in the school district. Although recommendations for regularly screening male adolescents for chlamydia have not been developed, the rate of acquisition of a new infection in this study indicates that in areas with high prevalence of STDs, annual chlamydia screening for adolescent males may be indicated.

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EVALUATING NONINVASIVE MARKERS OF FIBROSIS IN A SOUTHERN POPULATION OF HEPATITIS C INFECTED VETERANS

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Purpose of Study: Liver biopsy is the standard for assessment of fibrosis in chronic hepatitis. Limitations of sampling error and variability of interpretation of this costly, invasive procedure have resulted in the development of serum markers of fibrosis, such as the aspartate aminotransferase (AST) to platelet ratio index (APRI). The APRI score has not been validated in a predominantly African American population with chronic hepatitis C in the Southeastern United States.

Methods Used: The hepatitis C clinics at the Veterans Affairs Medical Center in Jackson, Mississippi provide care to over 1000 patients with chronic hepatitis C infection annually. The clinic population is 70% African American and 92% male. Using ICD-9 codes, 68 patients with chronic hepatitis C infection who had received a liver biopsy were identified. The APRI score ($[\text{AST}/\text{ULN}]/[\text{Platelet}] \times 100$) was calculated using laboratory tests corresponding to the dates of biopsy. Liver histopathology was classified using the modified Knodell's score (F0-no fibrosis; F1-portal fibrosis without septa; F2, few septa; F3, numerous septa without cirrhosis; F4-cirrhosis). Data was entered into SPSS v. 18.0 and analyzed using SAS v. 9.1.

Summary of Results: All patients were male; half (50.63%) were African American. Thirty eight patients had liver biopsies with absent to mild fibrosis (F0-F1). On logistic regression, the APRI score independently predicted the fibrosis score ($p < 0.001$). The area under the curve (AUC) of the receiver operator characteristics were used to determining optimal cut-off values of the APRI score. An APRI score of ≤ 0.61 predicted mild fibrosis (F0-F1) with AUC 0.88 (95% CI, 0.80-0.97), with 86% sensitivity and 83% specificity. A cut-off of ≥ 1.01 predicted significant fibrosis/cirrhosis (F2-F4) with AUC of 0.97 (95% CI, 0.92-1), with 94% sensitivity and 90% specificity.

Conclusions: This small sample indicates the calculated APRI score corresponds to the degree of liver fibrosis in Southern populations with chronic hepatitis C infection. Further investigation in this population is warranted.

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RENAL ABSCESES DUE TO CAT SCRATCH DISEASE

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Case Report: A previously healthy 9 year old female presented with a 12-day h/o fever as high as 104F, associated with lethargy, fatigue & headaches. There was h/o exposure to cats, dogs & horses & travel to Colorado. On exam she was febrile but otherwise unremarkable. There was no palpable lymphadenopathy, hepatosplenomegaly or rash. Initial labs showed a WBC count of 14,200/cu mm with 68% segs, 9% lymphs, 11% bands, 10% monos & 2% eos. Hemoglobin was 13.1 mg/dL & a platelet count of 303,000/cu mm. ESR & CRP were elevated at 36 mm/h and 9.6 mg/dL, respectively. Heterophile antibody test, rapid Influenza test, & a throat culture for Group A β hemolytic streptococcus were all negative. Blood & urine cultures remained sterile. UA was normal. BUN was between 5 to 14 mg/dL & creatinine between 0.4 to 0.6 mg/dL during hospitalization. Fever persisted with daily spikes of as high as 103F & ESR & CRP increased to 135 mm/hr and 23 mg/dL, respectively. Abdominal & pelvic ultrasound, chest X-ray & cardiac echo were normal. 4 days after hospitalization she developed chills & a fever of 104F. Blood cultures were repeated & IV Vancomycin & Meropenem were started. She remained febrile on antibiotics. CT with contrast of the abdomen revealed multiple hypodense lesions scattered within the cortical portion of the parenchyma of kidneys bilaterally. Her antibiotic regimen was changed to IV Gentamicin & Rifampin on day 5 of hospitalization because of suspicion of cat scratch disease. Initial Bartonella serology was IgG 1:640 (negative <1:320) & IgM 1:100 (<1:40) one week later the IgG was >1:2560 & IgM was >1:800 & one month later IgG of 1:1024 & IgM of 1:40. She remained febrile during her 7 days of hospital stay although both the frequency and height of the fever spikes were lower & she appeared better overall. Her ESR & CRP decreased to 95 mm/hour & 9.1 mg/dL, respectively. Patient was discharged on IV Gentamicin & Rifampin. She was seen 9 days after discharge & was

afebrile, active & without any fatigue or headache. Her ESR & CRP two weeks after discharge were 16 mm/hr & <0.5 mg/dL, respectively. A repeat abdomen CT scan with contrast showed that the microabscesses had resolved. One month after discharge patient remained well & antibiotics were discontinued after 3 weeks.

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EXTRAPULMONARY TUBERCULOSIS AND HUMAN IMMUNODEFICIENCY VIRUS COINFECTION IN AN URBAN HOSPITAL SYSTEM

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Purpose of Study: The proportion of tuberculosis (TB) cases that are extrapulmonary (EPTB) has been increasing but there is limited data on risk for mortality among those with EPTB, especially in the U.S.

Methods Used: A retrospective chart review was performed of all adult cases of EPTB at Grady Memorial Hospital (an urban, university-affiliated hospital) in Atlanta, GA over a 12 year period (January 1995 through December 2007). Risk factors for all-cause mortality were identified in multivariate analysis using a log-binomial regression model.

Summary of Results: A total of 287 cases were identified. 68% were male, blacks composed 82% of all patients, and 47% were HIV co-infected. The mean age was 39 years, and 21% of patients were foreign-born. The most common sites of infection were lymphatic (26%), meningeal (21%), and pleural (17%). Median length of hospital stay for an EPTB patient was 10 days (mean 19.6 days). HIV-seropositive patients were significantly more likely to have disseminated EPTB than HIV-uninfected persons (30% vs. 12%, $p < .001$), and significantly less likely to have pleural EPTB (7% vs. 27%, $p < .001$).

All-cause mortality was 16% overall; HIV+ patients were significantly more likely to die than HIV-uninfected persons (25% vs. 9%, $p < .001$). In univariate analysis all-cause mortality was significantly associated with increasing age (PR=1.03 per year, 95%CI 1.01-1.04), male gender (PR=2.28, 95% CI 1.11-4.68), being U.S.-born (PR=3.72, 95% CI 1.20-11.59), HIV co-infection (PR=2.60, 95% CI 1.43-4.71), concomitant pulmonary TB (PR=2.20, 95% CI 1.28-3.78), and having meningeal (PR=2.77, 95% CI 1.36-5.64) or disseminated (PR=4.56, 95% CI 2.43-8.57) EPTB. In multivariate analysis, independent predictors of mortality included having meningeal (PR=2.48, 95% CI 1.22-5.04) or disseminated (PR=3.51, 95% CI 1.82-6.75) EPTB and HIV co-infection (PR=1.85, 95% CI 1.01-3.40).

Conclusions: EPTB was not an uncommon finding at our urban U.S. hospital. These cases often required long hospital admissions and were associated with substantial mortality, particularly among HIV+ persons and those with meningeal or disseminated disease.

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MYCOBACTERIUM TUBERCULOSIS-INDUCED ARGINASE II MAY SUPPORT BACTERIAL GROWTH IN MURINE MACROPHAGES

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Purpose of Study: Two key enzymes may regulate the host immune response to *Mycobacterium tuberculosis* (Mtb): inducible nitric oxide synthase (iNOS) and arginases, both capable of regulating L-arginine availability. The generation of nitric oxide (NO) is responsible for the toxicity of macrophages against bacterial pathogens, while the conversion of L-arginine to L-ornithine by arginase has been shown to support the intracellular survival of *H. pylori*, *Leishmania* spp. We believe that Mtb has developed similar survival strategies, which involve NO and L-arginine metabolism to enable the persistence of mycobacterial infection.

Methods Used: Raw 264.7 cells and alveolar macrophages were infected with Mtb (H37Rv) at 3:1 ratio. Arginase was tested by enzymatic assay and Western blot; amino acid content by HPLC, and mycobacterial growth by CFU in agar.

Summary of Results: We found that at concentrations of 10 µg/ml Mtb lysates significantly ($p < 0.01$) induced arginase activity after 72 hrs in culture and attributable to only arginase II. The levels of L-arginine significantly ($p = 0.013$) decreased but L-ornithine levels remained unchanged. An increase in

iNOS and NO was observed. In contrast, when Raw cells and murine alveolar macrophages were infected with live Mtb (H37Rv) at 3:1 ratio, a five fold increase in arginase II activity was observed at 24 hrs, and increase in L-ornithine and a decrease in NO production. These results suggest that L-ornithine increments by arginase II could promote polyamine synthesis blocking simultaneously NO production, therefore favoring Mtb intracellular growth. Treatment of Mtb-infected cells with arginase inhibitors significantly reduced Mtb growth inside the host cells. Infected cells produced high amounts of TNF α , TGF β , IL-6, IL-10 and GM-CSF. TGF β or IL-10 stimulation did not trigger arginase induction in these cells indicating that Mtb products are responsible for the induction of arginase II and possibly regulating iNOS and NO expression.

Conclusions: Understanding the mechanisms that regulate L-arginine metabolism and Mtb survival may enable us to design promising therapeutic strategies not only to treat active but also extensively drug resistant tuberculosis.

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A NOVEL CLINICAL PREDICTION RULE FOR MULTIDRUG-RESISTANT TUBERCULOSIS

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Purpose of Study: Multidrug-resistant tuberculosis (MDR-TB) is a worldwide public health problem. MDR-TB is defined as resistance to isoniazid and rifampicin. Culture and susceptibility testing (DST) are the primary mean for its diagnosis; however, they are expensive and scarce in developing countries. This study aimed to develop a clinical prediction rule (CPR) to stratify risk of MDR-TB among TB patients in endemic areas.

Methods Used: Patients with pulmonary TB were prospectively collected during a phase III trial in Lima, Peru (2004-2005). The reference standard was culture with DST. Variables explored were patient characteristics, prior TB, MDR-TB contact, symptoms, physical exam findings, and radiologic pattern (in a subset of patients). We used logistic regression to develop 2 models: clinical variables alone (Model 1) and added significant radiologic patterns (Model 2). Areas under receiver-operating curves (AUC) and used bootstrapping (2,000 times) were calculated. We also computed risk scores (OR <1 negative value and >1 positive value), and interval likelihood ratios (LR).

Summary of Results: A total of 898 patients were included, the prevalence of MDR-TB was 6.7%. Variables in Model 1 were productive cough, fever or night sweats, general malaise, prior TB, family member died of TB, MDR-TB contact, history of imprisonment, and systolic blood pressure (pseudo R² 0.05). Adding cavitory, alveolar, and mixed radiologic patterns (Model 2), increased modestly the utility of the explanatory model (pseudo R² 0.13). The AUC for Model 1 (0.67; 95% CI 0.59, 0.74) was lower than Model 2 (0.78; 95% CI 0.70, 0.88). The risk score stratified MDR-TB prevalence ($p < 0.001$), Table.

Conclusions: A clinical prediction rule including clinical and radiological patterns at presentation can stratify risk of MDR-TB. If further simplified and validated, such a rule may guide testing and treatment decisions in resource limited endemic areas.

Risk Score	N(%)	MDR-TB Prevalence	Interval LR (95% CI)
≤-5	477 (72%)	2.1%	0.40 (0.23 - 0.63)
>-5 to <15	161 (24%)	9.9%	2.05 (1.34 - 2.87)
≥15	29 (4%)	27.6%	7.10 (3.34 - 14.12)

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PREVALENCE AND RISK FACTORS FOR EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS AND OTHER SECOND LINE DRUG RESISTANCE AMONG PATIENTS STARTING TREATMENT FOR MULTIDRUG RESISTANT TB IN THE COUNTRY OF GEORGIA

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Purpose of Study: To determine the prevalence of resistance to first- and second-line drugs (SLDs) among patients with multidrug-resistant TB (MDR-TB) started on therapy with SLDs in the country of Georgia in 2008.

Methods Used: Drug susceptibility tests (DSTs) were performed using the absolute concentration method on Lowenstein-Jensen medium with the exception of pyrazinamide susceptibility testing which was performed using the MGIT960.

Summary of Results: There were 284 patients that had MDR-TB (isolates resistant to at least both isoniazid [INH] and rifampin [RIF]). Among those with MDR TB, 27 (9.5%) had evidence of extensively drug-resistant (XDR)-TB (i.e., resistant to at least INH and RIF, plus resistance to a fluoroquinolone and any injectable SLD [capreomycin, kanamycin or amikacin]). Of 284 patients with MDR-TB, 203 (72%) were male; median age was 37 years. The large majority of patients had pulmonary TB - 260 (91%), 3 (1%) had extrapulmonary TB, 10 (4%) had pulmonary and extrapulmonary TB, and 11 (4%) had missing information on site of TB disease. Among MDR-TB cases, 18 (6.3%) were newly diagnosed cases (primary drug resistance), 185 (65.1%) were previously treated with first-line drugs only, 65 (22.9%) were previously treated with second-line drugs (even those these were not available through the National TB Program [NTP]), and 16 (5.6%) had unknown treatment history. Among 284 MDR-TB isolates, 100% were resistant to INH and RIF, 97% to streptomycin, 66% to ethambutol, 69% to pyrazinamide, 35% to kanamycin, 24% to capreomycin, 19% to ofloxacin, and 14% to PAS. Prior treatment with SLDs was associated with increased risk for XDR-TB (PR=4.37, 95% CI 2.04-9.37).

Conclusions: The prevalence of resistance to first- and second-line drugs was high among those with MDR-TB in Georgia. Nearly 10% of those with MDR-TB had XDR-TB and prior treatment with SLDs the major risk factor for XDR-TB. Effective use and control of SLDs is critical, especially given that XDR-TB developed prior to availability of SLDs through the Georgia NTP.

Perinatal Medicine II Concurrent Session

1:00 PM

Saturday, February 27, 2010

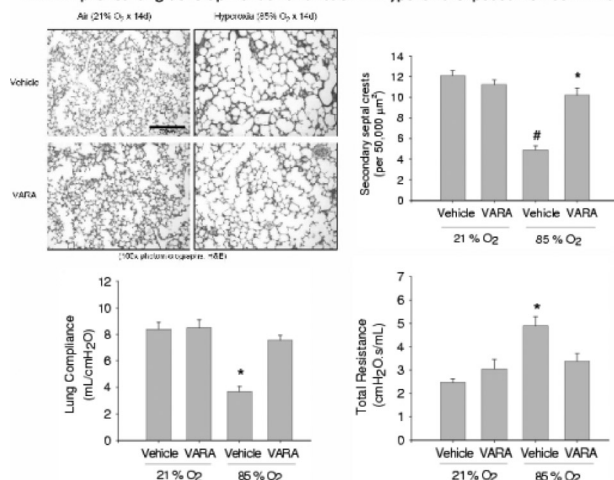
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RETINOIDS ATTENUATE HYPEROXIA EFFECTS ON NEWBORN MOUSE LUNG

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Purpose of Study: Bronchopulmonary dysplasia in preterm infants is characterized by inhibition of lung alveolar development associated with increased pro-inflammatory cytokines. Clinical trials indicate Vitamin A (VA) supplementation decreases BPD and/or death. VA is metabolized into retinoic acid (RA). We have previously shown that a 10:1 molar combination of VA and RA (VARA) synergistically increases lung retinol content in newborn mice. We hypothesized that this biochemical synergistic effect translates into functional benefits in attenuating hyperoxia-induced effects on the newborn lung.

VARA improves lung development and function in hyperoxia-exposed newborn mice



Methods Used: Newborn C57BL/6 mice were exposed to hyperoxia (85% O₂) or room air for 7 or 14 days and given vehicle or VARA. Lung retinol content was measured by HPLC, lung function was assessed by flexiVent, and lung development was evaluated by morphometry. A panel of cytokines were evaluated by a qPCR array and by ELISA in lung homogenates.

Summary of Results: VARA attenuated the hyperoxia-induced inhibition of alveolarization and improved lung function, with higher compliance and lower resistance (Figure). VARA also attenuated the hyperoxia-induced increases in macrophage inflammatory protein -2 α (MIP-2 α ; Cxcl2) and interferon-gamma (IFN- γ) mRNA and protein.

Conclusions: VARA improved lung development and function, and reduced pro-inflammatory cytokines in newborn mice exposed to hyperoxia. Studies are in progress to determine how retinoids regulate MIP-2 α and IFN- γ .

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UREAPLASMA INTRA-AMNIOTIC INFECTION IN A RHESUS MACAQUE MODEL BLUNTS VILLUS DEVELOPMENT AND INDUCES MUCOSAL INFLAMMATION IN THE FETAL INTESTINE

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Purpose of Study: Maternal chorioamnionitis is a risk-factor for necrotizing enterocolitis in term infants. We used a rhesus macaque model to investigate whether intra-amniotic Ureaplasma infection alters normal development of the crypt-villus architecture and immune cell populations in the fetal intestine.

Methods Used: Chorioamnionitis was induced in rhesus macaques by intra-amniotic inoculation (IAI) of *U. parvum* (serovar 1, 10(7) cfu) or media (controls, n=3 each) on day 123-125 (term=168 days); fetuses were exposed to *U. parvum* for up to 14 days (n=3). Some mothers were then treated with azithromycin (AZI; 25/mg/kg, q12h; iv, n=4) for 10 days. Cesarean delivery was performed at the onset of preterm labor (range: 140-150 dGA) and at a comparable gestation in controls. Computer-assisted measurements of villi, lamina propria (LP), crypts, and intestinal epithelial cells (IEC) were made. We enumerated cells expressing CD3, CD14, CD11b, CD11c, HAM56, and MPO in LP and sought TLR4 and TNF- α immunoreactivity in HAM56+ macrophages.

Summary of Results: Intra-amniotic infection was associated with altered crypt-villus development in fetal intestine: decreased villus height (300 $\pm$ 13 vs. 459 $\pm$ 17 μ m in control), villus area (43869 $\pm$ 7548 vs. 68963 $\pm$ 4447 μ m² in control), LP area (13115 $\pm$ 1258 vs. 32190 $\pm$ 2462 μ m²), fewer LP cells (41 $\pm$ 8 vs. 59 $\pm$ 4/villus), and smaller crypt area (2259 $\pm$ 856 vs. 5491 $\pm$ 258 μ m²); all p<0.05. Despite reduction in LP cells, *U. parvum* IAI was associated with increased number of HAM56+ macrophages (18 $\pm$ 2 vs. 4 $\pm$ 1/villus in control, p<0.001) and CD11c+ (26 $\pm$ 2 vs. 6 $\pm$ 2/villus in control, p<0.001) myeloid dendritic cells. In contrast to macrophages in control intestine, macrophages in *U. parvum* exposed animals appeared activated (enlarged, increased granularity) and expressed TLR4 and TNF- α . These changes were not reversed by AZI therapy.

Conclusions: Intra-amniotic infection with Ureaplasma inhibited villus development in the fetal intestine and recruited activated macrophages and dendritic cells to the lamina propria. These fetal changes were not reversed by maternal antibiotic therapy, despite eradication of *U. parvum* from the amniotic fluid within 3-4 days.

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UREAPLASMA INCREASES MATRIX METALLOPEPTIDASE 9 IN THE FETAL MOUSE LUNG

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Purpose of Study: Antenatal Ureaplasma infections is a risk factor for Bronchopulmonary Dysplasia (BPD) in the preterm infant. BPD is characterized by abnormalities in terminal airway branching and alveolarization. In the developing lung, collagenases Matrix Metalloproteinase's (MMP) 9 & 2 remodel the extracellular matrix scaffold thus allowing normal branching morphogenesis. We speculate that Ureaplasma alters collagenase expression in fetal lungs contributing to the BPD phenotype. To test this we hypothesized that Ureaplasma alters expression and activity of MMP9 and MMP2 in the fetal mouse lung.

Methods Used: Lung explants were isolated from E15 mice and cultured with or without *Ureaplasma parvum* or Pam2CSK4, a synthetic diacylated lipopeptide with activity similar to the macrophage stimulatory activity of *Ureaplasma*. Primary fetal lung fibroblasts and a murine lung alveolar epithelial cell line (MLE-12) were cultured and treated with either *Ureaplasma* or the peptide. Gene expression was quantified using real time PCR. Activity of secreted MMP9 and MMP2 was measured using gelatin zymography.

Summary of Results: *Ureaplasma* treatment resulted in a 6.7 fold increase in MMP9 mRNA expression in fetal mouse lung explants ($P < 0.05$). Pam2CSK4 also increased explant MMP9 mRNA expression compared to control (100ng/ml- 6 fold increase, 200ng/ml - 9 fold increase; $P < 0.05$). MMP2 mRNA expression was unaffected by either treatment. To test if both the fetal lung mesenchyme and the alveolar epithelium were involved in the up-regulation of explant MMP9, we cultured primary fetal lung fibroblasts and MLE-12 cells. *Ureaplasma* and Pam2CSK4 increased MMP9 mRNA expression in primary lung fibroblasts (50.2 fold increase, $P < 0.05$) but not in MLE-12 cells. In preliminary zymography experiments we have found MMP9 but not MMP2 secreted activity to be increased in explants and in fetal lung fibroblasts treated with Pam2CSK4 or *Ureaplasma*. This awaits confirmation in future experiments.

Conclusions: In fetal mouse lung explants and cultured fibroblasts, *Ureaplasma* and Pam2CSK4 increase MMP9 mRNA expression. We speculate that increased MMP9 by altering extracellular matrix deposition and degradation may contribute to the altered lung development seen with antenatal *Ureaplasma* infections.

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IL-1 STIMULATES EPITHELIAL SODIUM CHANNEL REGULATION IN LUNG EPITHELIAL CELLS.

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Purpose of Study: In preterm infants inflammation-induced fetal lung maturation occurs as a consequence of intra-amniotic exposure to pro-inflammatory cytokines e.g. IL-1 and correlates with a decreased incidence of respiratory distress syndrome(RDS). Accelerated maturation of epithelial sodium channels (ENaC) may also alleviate the onset of RDS by increasing perinatal lung fluid clearance. ENaC is a multimeric protein consisting of α , β , and γ subunits, with the α -subunit being critical for Na^+ transport in the lung. The objective of this study is to determine the effects of IL-1 α and β on regulation of ENaC subunit expression in a mouse lung epithelial (MLE-12) cell line.

Methods Used: MLE-12 cells were exposed to IL-1 α or IL-1 β (200pg/ml). Immunoblotting was employed to detect changes in protein levels compared to control cells or adult mouse lung. RT-PCR was used to determine α -ENaC mRNA expression. Biotinylation experiments were performed to determine the abundance of α -ENaC localized at the cell surface.

Summary of Results: α , β , and γ -ENaC subunits are minimally expressed in control MLE-12 cells compared to adult mouse lung. Compared to control cells, levels of α -ENaC protein in MLE-12 cells were increased after exposure for 24h to either IL-1 α or β (2.9 and 3.1-X, respectively) and showed a slight reduction after 48h. IL-1 α and IL-1 β also induced a significant increase in α -ENaC mRNA expression after 24h but markedly decreased after 48h. IL-1 α and IL-1 β transiently elevated cell-surface expression of α -ENaC protein which peaked after 24h but was decreased by 48h. γ -ENaC protein levels were also increased after 24h but minimal changes were observed with β -ENaC. IL-1 α and β -dependent increases in α -ENaC protein were significantly attenuated by cycloheximide and an IL-1 receptor antibody. Inhibition of ERK 1,2 MAP kinase by PD98059 and p38 MAP kinase by SB203580 decreased both IL-1 α and β -induced α -ENaC protein expression.

Conclusions: Exposure of MLE-12 cells to IL-1 α or IL-1 β stimulates expression of α - and γ -ENaC after 24h. Increases in α -ENaC protein formation by MLE-12 cells in response to IL-1 α and IL-1 β also involve activation of MAPK pathways.

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THE ONTOGENESIS OF THE ENDOCRINE PANCREAS IN THE PREMATURE BABOON MODEL

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Purpose of Study: Transient neonatal hyperglycemia has been reported in up to 80% of extremely premature infants. The pathogenesis of this condition is not fully understood, but insulin resistance and decreased insulin secretion have been implicated. The morphology of the pancreas during early stages of development is not clearly defined. It is known that impaired islet cell mass and function determine the development of diabetes. Therefore, the purpose of this study is to determine the morphology of the fetal baboon pancreas at varying gestations. We hypothesize that the preterm endocrine pancreas is unorganized and that cellular differentiation is not fully developed.

Methods Used: Twelve fetal baboons were delivered via c-section at 125 day(d) gestational age (GA), 140d GA, or 175d GA and four animals were delivered vaginally at term (185d). All animals were euthanized shortly after birth. Pancreas tissue was obtained and immunohistochemistry was performed for insulin, glucagon, somatostatin, and synaptophysin. Relative volumes and absolute masses of the different microscopic structures were calculated utilizing the Computer Assisted Sterology Toolbox 2.0 system. ANOVA was utilized to assess significance (SPSS 11.5).

Summary of Results: The relative volumes and absolute masses of the islets as well as the alpha, beta, and delta cells were quantitatively similar when compared across the different GA. The percent of beta cell mass was similar to alpha and delta cell mass within each GA. Qualitatively, the pancreatic islets and endocrine cell subsets became increasingly organized as gestational age advanced.

Conclusions: No differences were seen in the relative volumes and absolute masses of the pancreatic islets or in the primary hormone producing cells when compared across GA in the preterm-term baboon. The percent of beta cell mass was similar to alpha and delta cell mass, contrasting to the higher beta cell mass seen in healthy children and adults. As suspected, pancreatic islets became more organized with increasing GA. These findings suggest that the premature endocrine pancreas is not fully developed which may play a role in the pathogenesis of hyperglycemia of prematurity. Further work is ongoing to determine single cell volumes and hormone production by Electron Microscopy.

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HOW MUCH DO PARENTS OF NICU PATIENTS UNDERSTAND ABOUT THEIR INFANTS' DISEASE PROCESSES AND THEIR POTENTIAL IMPACT ON FUTURE HEALTH STATUS?

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Purpose of Study: We sought to determine the health literacy of NICU parents with regard to their infant's disease processes and the potential impact on future health status. Having an infant in a Neonatal ICU can be an extremely stressful experience. Stressors include the infant's precarious conditions, complicated technology, uncertainties about future health and difficulties understanding the complicated disease processes of prematurity. Good neonatal care requires open communication between the healthcare team and parents. But before we can improve, we need to evaluate how much parents comprehend in our current model.

Methods Used: Parents of fifteen VLBW infants (BW<1500g) were given a survey between three and four weeks of life and again prior to discharge to determine 1) how much the parent understood about their infant's current health problems and 2) possible affects of these problems on future health status. We also asked where they found the best information on their infant's health. The infants' charts were then reviewed to correlate the accuracy of parental understanding with actual patient diagnoses.

Summary of Results: Parents correctly identified major issues in 85% of the first surveys and 91% in the second. Gastrointestinal, neurological and infectious disease processes appear the best understood (all averaging >90% accuracy). Hematological and ophthalmologic issues were least recognized, just 43% and 29% were identified at discharge, respectively. Only 23% of parents expected their child to have permanent health sequelae of prematurity. Of those, 63% felt the effects would be minimal. Refreshingly, 89% of parents felt they understood 'a great deal' of what happened with their infant. Doctors (47%) and nurses (44%) were cited as the best information sources.

Conclusions: This preliminary data suggests that NICU parents have good understanding of the major health issues affecting their children. In our unit, we could improve upon explaining hematological and ophthalmologic problems. The majority of parents of VLBW infants expect their child to have minimal, if any, permanent health issues due to prematurity. We are

continuing to survey the same parents at yearly intervals to find out if their health literacy improves as their child grows.

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HUMAN MILK ANALYSIS FOR CRITICALLY ILL INFANTS: A USEFUL ADJUNCT TO NUTRITIONAL MANAGEMENT IN VLBW (<1500 g) INFANTS?

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Purpose of Study: To analyze single milk samples for macronutrients (protein, fat, carbohydrate) using a mid-infrared milk analyzer, adapted from the dairy industry for HM analysis.

Methods Used: This study was approved by the University of Louisville IRB and the Norton Hospital Research Office prior to initiation. Waste samples from daily milk preparations were obtained from the NICU formula prep room. Samples were warmed to 42° C for 10 minutes prior to analysis. The Calais Milk Analyzer (Metron Instruments, Solon, OH), previously calibrated with confirmed-content human milk samples, was zeroed with water prior to each day's run. Individual samples were analyzed for nutrient content; energy (kcal/ounce) was derived from those results. Lactose values do not include oligosaccharides. Single sample analysis took less than 1 minute. Descriptive statistics are provided.

Summary of Results: Ninety-nine discrete milk samples from 24 women were analyzed. The mean nutrient values were: protein 1.5 ± 0.3 gm/dL, lactose 5.2 ± 0.6 gm/dL and fat 3.7 ± 1.1 g/dL. Mean calculated energy content was 16.9 ± 2.8 kcal/oz. Individual women produced milk samples with protein concentrations ranging from 0.9 to 2.3 g/dL and fat from 1.5 to 7.6 g/dL; energy content varied from 10.5 to 26.2 kcal/ounce.

Conclusions: The Calais analyzer can be used to measure macronutrient content in single human milk samples. Mean values for protein, lactose and fat compare well with published values. There were wide variations in individual milk profiles. Assessment of individual maternal milks may be useful to address the mother-to-mother variability and guide fortification in order to maximize nutrient provision to VLBW infants during a period of accelerated growth.

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SWALLOW-BREATH INTERACTION IN LOW-RISK PREMIES AND INFANTS WITH BPD

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Purpose of Study: We have identified 3 types of swallow-breath interactions (Sw-Br) during nonnutritive suck (NNS) in low-risk preterm (LRP) infants: central apnea (CA), obstructive apnea (OA) and attenuated respiration (AR). We have not investigated if/how BPD interferes with Sw-Br progression. This project will describe differences in Sw-Br during NNS among LRP and BPD infants.

Methods Used: Multi-channel graphs of NNS were collected with attention to swallow pressure, airflow, and chest motion. LRP infants were born at <35 weeks, no grade 3/4 IVH, no congenital anomalies and not likely to develop BPD. Infants likely to develop BPD were randomized to receive or not receive a speech therapy intervention (BPDwithTX, BPDnoTX). Gestational age (GA), birth weight (BWT), gender, weeks before first nipple feed (WBFN), weeks since first nipple feed (WSFN), and number of swallows (SW) were compared against the 3 types of Sw-Br.

Summary of Results: There were 176 swallows in the LRP group (35 studies, 16 infants). In the BPDnoTX group there were 135 swallows (31 studies, 15 infants). In the BPDwithTX group there were 76 swallows (20 studies, 11 infants). In the LRP group, significant relationships (p<0.05) were noted for AR with WSFN (OR=1.6), OA with male gender (OR=0.4), GA (OR=1.3) and WSFN (OR=0.7). A relationship for CA with WBFN was not quite significant (p=0.0584). Significant relationships for infants in the BPDnoTX group were for CA with SW (OR=0.8) and OA with SW (OR=1.4). In the BPDwithTX group, a relationship between OA and BWT was not quite significant (p=0.0554). When the BPD groups were combined, there were significant relationships for AR with SW (OR=0.9) and OA with SW (OR=1.2).

Conclusions: There are predictable changes in Sw-Br interaction that occur in LRP infants during NNS that are not present in infants with BPD. This is consistent with other studies of infant feeding in which infants with BPD have dysmature development and may help describe the contributions of maturation and development to infant feeding.

This work was supported by NIH Grant 5 K23 HD 050581.

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FECAL MICROBIOTA IN INFANTS WITH AND WITHOUT NECROTIZING ENTEROCOLITIS

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Purpose of Study: Necrotizing enterocolitis (NEC) is an invasive inflammatory disease of the neonatal bowel with high morbidity and mortality. The etiology of NEC is unclear, but there is strong evidence supporting bacterial colonization as a major risk factor. The purpose of this study was to analyze and compare the fecal microbiota of infants who develop NEC with those of age- and gestational age-matched controls using sensitive molecular biological techniques and to correlate fecal microbiota data with development or non-development of NEC.

Methods Used: After obtaining parental consent, sequential stool samples were collected from 172 premature infants ≤ 1500 grams or ≤ 34 weeks of gestation. To date, DNA has been extracted from 18 stool samples (including from 1 child with active NEC), and PCR amplification of 16S rRNA genes was undertaken prior to 454 Pyrosequencing to determine DNA sequences. Online bioinformatics search tools were used to identify microorganisms based on their 16S rDNA sequences. Clinical chart reviews were performed to provide clinical data for correlation with genetic parameters.

Summary of Results: Bacteria were identified predominantly within 2 phyla (Proteobacteria and Firmicutes) and 5 genera (unclassified Citrobacter, Enterobacter, Enterococcus, Staphylococcus, and Streptococcus). Microbial diversity increased with age. Compared with controls, the infant with active NEC exhibited decreased diversity with a predominance of Enterococcus spp., which are organisms that exhibit adhesive, cytolytic and proteolytic capabilities that may predispose to the development of NEC.

Conclusions: These findings suggest that fecal microbiota in the premature infant vary with age and that bacterial diversity is decreased during active NEC. There is not enough data yet to comment on effects of diet and antibiotic use. Supported by the Louisiana Vaccine Center and the South Louisiana Institute for Infectious Disease Research sponsored by the Louisiana Board of Regents.

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THICKENED FEEDS IMPROVE ORAL FEEDING TOLERANCE IN GROWING PREMATURE NEWBORNS

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Purpose of Study: Swallowing dysfunction and delay of oral feeding skills in premature newborns (NB) significantly delay discharge from the nursery. We hypothesize that thickening formula or expressed breast milk with Simply Thick[®] will eliminate or reduce the symptoms of oral feeding dyscoordination.

Methods Used: Healthy NB between 32 and 40 weeks adjusted gestational age receiving four or more PO feeds and experiencing symptoms of bradycardia, O₂ desaturations, choking, or apnea were enrolled. Serving as their own control, each NB received PO feeds thickened to nectar consistency. It was important that nipple orifice size did not change. Each NB was subsequently monitored for feeding-associated symptoms over 2 days or 8-16 PO feeds. If symptoms continued over the course of 3 feeds, thickening was increased to honey consistency. After the 2 day trial of thickening, thickener was removed and symptoms again monitored during PO feeds. Each NB study was completed after monitoring PO feeds for 2 more days, and thickener was returned to PO feeds if symptoms reoccurred or worsened.

Summary of Results: 15 NB (mean adjusted gestational age 35.4 wks) were enrolled after consent. Significantly, 12/15 were male. With the addition of thickener to feeds, symptoms were eliminated in 7/15 NB and improved in

the other 8/15 NB. Bradycardias decreased from $44 \pm 26\%$ to $5 \pm 5\%$ of feeds ($p < 0.001$), and O_2 desaturations decreased from $18 \pm 23\%$ to $4 \pm 7\%$ ($p = 0.024$). Though decreased, other symptoms were too infrequent to demonstrate statistical significance. Upon removal of thickener, symptoms resumed for 10/15 NB. Though symptoms self-resolved in 5/15 NB and may have done so even in the absence of thickener, the demonstrated efficacy of the thickener in reducing or eliminating symptoms remained significant for the group at large ($\chi^2 = 12.00$, $p = 0.007$). No adverse events were observed, and 10/15 NB were discharged home on thickened feeds.

Conclusions: Thickening formula or expressed breast milk with Simply Thick® does eliminate or reduce the symptoms associated with oral feeding dyscoordination observed in growing, premature NB. We speculate that earlier discharge from the hospital will be made possible by thickening PO feeds for NB with associated symptoms - most commonly bradycardia and O_2 desaturations.

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VAV2 IS TYROSINE PHOSPHORYLATED IN HUMAN AND BOVINE PULMONARY VASCULAR ENDOTHELIAL CELLS STIMULATED WITH BACTERIAL LIPOPOLYSACCHARIDE (LPS) AND CYTOKINES

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Purpose of Study: We sought to determine whether pulmonary vascular endothelial cells expressed vav family members and whether these vav proteins were tyrosine phosphorylated during activation of these cells by LPS and host cytokines. Previous work from our laboratories had implicated the role of vav1 protein in the upregulation of nitric oxide (NO) production in macrophages.

Methods Used: We studied bovine pulmonary artery endothelial cells (bPAECs) and human pulmonary microvascular endothelial cells (hPMVECs) (primary cells, purchased from Lonza) cultured in Lonza's proprietary media. Cells were grown to confluence and stimulated with LPS, interleukin-1, tumor necrosis factor and interferon-gamma ("Cytomix") for 1-18 hours. Previous work has shown that Cytomix induces NO production by these pulmonary endothelial cells under these conditions. We used immunoblotting with rabbit polyclonal antisera specific for total vav1, vav2, or vav3, or for vav2 phosphorylated on tyrosine 174 to determine whether these lung endothelial cells expressed any of these vav family members.

Summary of Results: We found that both bPAEC and hPMVEC expressed vav2 (but not vav1 or vav3) protein by immunoblotting of whole cell lysates. Furthermore, after stimulation with LPS and a combination of cytokines ("Cytomix"), we found that vav2 becomes phosphorylated on tyrosine 174 within 1-2 hours in both bPAEC and hPMVEC. Maximum tyrosine phosphorylation of vav2 was observed at approximately 4 hours.

Conclusions: We found that vav2 was expressed in both human and bovine pulmonary vascular endothelial cells and was tyrosine phosphorylated after activation of these cells with LPS-containing "Cytomix". Vav2 may be an important target of SFKs in lung vascular endothelial cells exposed to bacterial products and host cytokines and may play a role in the regulation of NO production in these cells.

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ROLE OF INTERLEUKIN-23 IN HOST DEFENSE AGAINST PNEUMOCYSTIS CARINII INFECTION

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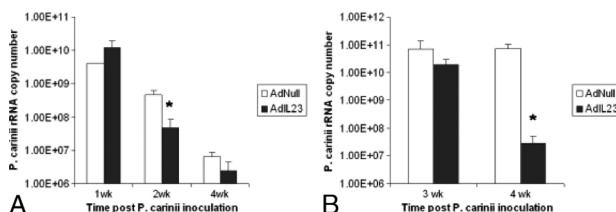
Purpose of Study: Host defense mechanisms against *P. carinii* are not fully understood, but pulmonary recruitment of CD4+ T-cells is critical for successful host defense against infection. CD4+ T-cells can be divided into

Th1, Th2 and Th17 subsets. IL-23 functions to maintain and expand the Th17 T-cell population. Previous work has shown that *P. carinii* stimulates the early release of IL-23 in the lung. Our study tested the hypothesis that local delivery of IL-23 can accelerate clearance of the *P. carinii* infection in normal and CD4+ depleted mice.

Methods Used: Normal and CD4+ depleted BALB/c mice were intratracheally injected with an adenoviral vector encoding IL-23(AdIL-23) or an empty vector (AdNull). Three days later, mice were intratracheally challenged with *P. carinii*. Mice were sacrificed at serial time intervals after challenge. The right lungs were homogenized in Trizol for RNA isolation and the left lungs were homogenized in PBS containing 0.5% Triton X-100 for protein analysis. The burdens of *P. carinii* in the lungs were determined by real time RT-PCR for *P. carinii* rRNA copy number. Protein levels of IL-23, IL-17, and IL-22 in lung homogenates were determined by ELISA.

Summary of Results: In normal mice (Panel A), AdIL-23 treatment significantly reduced fungal burden when compared to the control at 2 wk post infection. In CD4+ depleted mice (Panel B), AdIL-23 treated mice showed a significantly lower *P. carinii* burden than the AdNull treated controls at 4 wk post infection. In vitro, stimulation of CD4+ and CD8+ T cells with rIL-23 induced IL-17 and IL-22 production. In vivo, intracellular staining showed both CD4+ and CD8+ T cells in the lungs produced IL-17 and IL-22 in response to *P. carinii* infection.

Conclusions: We conclude that local delivery of IL-23 can accelerate clearance of *P. carinii* infection in normal mice and restore clearance of infection in CD4+ depleted mice. We speculate that this effect is mediated through enhanced production of IL-17 and IL-22 in pulmonary lymphocytes.



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INHALED STEROIDS AND INNATE DEFENSE AGAINST BACTERIAL PNEUMONIA

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Purpose of Study: Inhaled corticosteroids (ICS) are commonly used to treat COPD. Recent clinical trials show an increased risk of pneumonia in COPD patients treated with the inhaled steroid fluticasone propionate (FP). Due to the lack of published research describing effects of ICS on lung host defense, we designed experiments to test the hypothesis that treatment with inhaled FP impairs innate pulmonary host defense against bacteria.

Methods Used: C57BL/6 mice received nebulized FP at a concentration of 300µg/mL (or vehicle control) 20 minutes daily for 8 days. After 8 days, mice were intratracheally injected with 1×10^4 CFU *Klebsiella pneumoniae* (serotype 43816.) Infected mice received nebulized exposures for 10 additional days and survival was noted. In other experiments, animals were sacrificed at 24 & 48 h after infection to determine bacterial burden in lungs and blood. Leukocyte recruitment into lungs and alveolar macrophage phagocytosis of *K.pneumoniae* were studied in vivo to explore potential mechanisms of FP's effect on innate defense. Lastly, effects of FP on alveolar macrophage expression of nitric oxide and hydrogen peroxide were assessed in response to inflammatory stimuli in vitro.

Summary of Results: Exposure to inhaled FP conferred a survival disadvantage to mice infected with *K. pneumoniae*. Decreased survival was associated with increased bacterial burden in lungs at 24 & 48 h after infection and blood at 48 h. Inhaled FP had no effect on leukocyte recruitment into infected lungs, nor did it decrease the in vivo phagocytic ability of alveolar macrophages. In vitro, FP treatment decreased alveolar macrophage expression of nitric oxide but not hydrogen peroxide.

Conclusions: Inhaled FP impairs pulmonary clearance of *K. pneumoniae* in mice, which results in greater systemic bacteremia and death. Decreased

alveolar macrophage nitric oxide expression may impair intracellular bacterial killing, leading to more severe infection. These results support the study of ICS effects on the antimicrobial functions of human alveolar macrophages, particularly in COPD patients.

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THYMOPOIETIC PRECURSOR CELL PRODUCTION BY BONE MARROW IN RESPONSE TO PNEUMOCYSTIS INFECTION

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Purpose of Study: Pneumocystis carinii (PC) causes severe pneumonia in HIV-infected patients. CD4⁺ T cells play a key role in host defense against PC infection. Our previous experiments have shown that thymopoiesis is activated in mice during PC infection. In the thymus, all T cells are derived from earliest thymic progenitors originating in bone marrow. CCR9 positive multi-potent progenitors (CCR9+MPPs) bearing the lineage-c-kit+Sca-1+CD34+Thy1.1-CCR9+VCAM-1- surface markers in the bone marrow have been identified as the precursors of the earliest thymic progenitors. In this study, we investigated the activity of CCR9+MPP production in the bone marrow during the host response to PC infection in mice.

Methods Used: PC infection in the lung was induced by intratracheal injection of PC (2×10^5 /mouse) in male C57BL/6 mice. The animals were sacrificed 1, 2, 3, 4, 5 and 6 weeks following PC infection. In another set of experiments, nucleated bone marrow cells isolated from naïve mice were cultured for 16 hours in the absence and presence of PC extracts or different Toll-like receptor ligands. Bone marrow production of CCR9+MPPs was determined by flow cytometry.

Summary of Results: PC infection caused a significant increase in the number of CCR9+MPPs in the bone marrow. This increase in the number of marrow CCR9+MPPs reached the peak value between 3 and 4 weeks following PC infection. The number of CCR9+MPPs in the peripheral circulation was also increased along with the enhanced production of these precursors in the bone marrow. In vitro culture of bone marrow cells with PC extracts resulted in an increase in the number of CCR9+MPPs in the culture system. Stimulation of cultured bone marrow cells with ligands to TLR2 (zymosan), TLR4 (E. coli LPS), or TLR9 (ODN M362) each caused an increase in the number of CCR9+MPPs in the culture system.

Conclusions: During PC infection, the bone marrow increases production of thymopoietic precursor cells to support the thymopoietic response and lymphocyte recruitment to lung tissue. TLR signaling plays an important role in mediating the enhancement of thymopoietic precursor cell production in the bone marrow during this response.

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ESTROGEN TREATMENT FOLLOWING BURN INJURY REDUCES LUNG INFLAMMATION

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Purpose of Study: Burns remain a significant cause of injury and death in the United States. Approximately 500,000 patients are treated annually of which 40,000 become hospitalized. Increased morbidity and mortality in these patients are caused by complex processes stemming from uncontrolled secretion of inflammatory mediators. Patients with severe burn injury experience a rapid elevation in multiple circulating pro-inflammatory cytokines, with levels correlating with both injury severity and outcome. Accumulations of these cytokines in animal models have been observed in remote organs; however, data regarding early lung cytokine levels following burn injury and the effects of estrogen on these levels is lacking. Following severe burn injury, hyperaemia of the airway and increased edema are associated with both smoke inhalation and thermal injury in the lung. With respect to the latter, we studied the acute effects of a full-thickness third degree burn on the lung levels of TNF- α , IL-1 β , IL-6, and IL-10. In addition, we analyzed the effects of acute estrogen treatment on these cytokine levels. In this study, we hypothesized that acute estrogen treatment following burn injury in rats will significantly decrease the levels of pro-inflammatory cytokines.

Methods Used: Male rats received 40% total body surface area (TBSA) burns. Fifteen minutes following burn, the animals received a subcutaneous injection of either placebo (corn oil) or 17 β -estradiol (0.5 mg/kg). The animal

lungs were harvested at 0.5, 1, 2, 4, 6, 8, 12, 18, and 24 hours and the lung cytokine levels were measured using the ELISA method.

Summary of Results: Following burn injuries, the rats that were administered 17 β -estradiol had significantly ($p < 0.05$) lower IL-1 β (~60%), IL-6 (~80%), IL-10 (~70%), and TNF- α (~55%) cytokine levels in the lung compared to the placebo group.

Conclusions: 17 β -estradiol significantly decreases inflammation in the lung following severe thermal injury.

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REPETITIVE BLEOMYCIN LUNG INJURY RESULTS IN HYPERPLASTIC ALVEOLAR EPITHELIAL CELLS AND INCREASED EPITHELIAL MESENCHYMAL TRANSITION

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Purpose of Study: Current hypotheses suggest that chronic or repetitive lung injury is involved in the pathogenesis of idiopathic pulmonary fibrosis (IPF). Single dose intratracheal (IT) bleomycin is used extensively to induce experimental lung fibrosis. However, the fibrosis is transient and does not recapitulate the histologic features of usual interstitial pneumonia (UIP). Our goal was to develop a recurrent lung injury model using repetitive IT bleomycin that resulted in prominent type II alveolar epithelial cell (AEC) hyperplasia as in UIP.

Methods Used: Mice expressing Cre recombinase under the surfactant protein C promoter (SPC-Cre) were mated to R26Rosa-Stop-LacZ mice that have a loxP flanked STOP cassette upstream of lacZ. Here, Cre irreversibly activates β -galactosidase (β gal) expression in SPC⁺ epithelial cells, yielding a lung epithelium cell fate reporter system. Wild type C57BL/6J and cell fate reporter mice received IT bleomycin 0.04 units every other week for 8 doses. Mice were harvested at baseline, 2 weeks after a single dose, and 2 weeks after the last repetitive dose. Bronchoalveolar lavage (BAL), frozen tissue, and paraffin embedded tissue were collected.

Summary of Results: Compared to single dose, lungs of mice from the repetitive model had greater AEC apoptosis by TUNEL, less inflammatory cell influx by cell count on BAL fluid, and greater fibrosis. In the repetitive model, type II AEC hyperplasia was prominent, with many cells not only expressing pro-SPC, but also Clara Cell 10 (CC-10), suggestive of a bronchoalveolar stem cell (BASC) like population. Dual immunofluorescence for β gal and fibroblast markers S100A4 and vimentin, indicating fibroblasts derived via epithelial-mesenchymal transition (EMT), was more prominent in the repetitive model. Finally, even 10 weeks after the last repetitive bleomycin dose, lung fibrosis with hyperplastic AECs persisted.

Conclusions: Recurrent IT bleomycin results in marked lung fibrosis with prominent AEC hyperplasia, a pattern that persists well after the last dose of bleomycin. Taken together, this pattern is reminiscent of human forms of lung fibrosis, including IPF.

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NOVEL H1N1 INFLUENZA PNEUMONIA AND RESPIRATORY FAILURE. SINGLE CENTER EXPERIENCE, CASE SERIES AND REVIEW OF LITERATURE ON PERFORMANCE CHARACTERISTICS OF RAPID SCREENING TESTS FOR THE NOVEL H1N1 INFLUENZA VIRUS

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Purpose of Study: To describe the clinical characteristics of five patients with novel H1N1 influenza infection who progressed to respiratory failure and ARDS, and to review the literature on performance characteristics of rapid screening tests for the novel H1N1 influenza virus.

Methods Used: Charts abstracted and literature reviewed.

Summary of Results: Table 1 summarizes the clinical characteristics of the five cases with respiratory failure due to H1N1 virus. Review of literature revealed that the rapid antigen tests and DFA are relatively insensitive to detect the H1N1 virus, that the reported sensitivity for the rapid antigen tests vary from as low as 18% to as high as 69%, and that the sensitivity of DFA varies from as low as 47% to as high as 93%, depending on the type of kit used and the patient characteristics in the series.

Conclusions: Relying on negative rapid antigen tests and DFA to exclude infection with the novel H1N1 influenza virus can delay the diagnosis and

institution of appropriate therapy of this infection. We suggest that a negative rapid influenza test not be used to exclude the diagnosis of H1N1 infection in immunocompromised patients with clinical characteristics suggestive of an influenza infection. We further suggest that these critically ill patients be treated with oseltamivir or zanamivir while awaiting a more definitive diagnosis using viral cultures and/or PCR.

TABLE 1

AGE/SEX	COMORBID CONDITIONS	PRESENTATION	RAPID INFLUENZA TEST	VIRAL CULTURE	H1N1 PCR	INFLUENZA TREATMENT	OUTCOME
26 F	Lung transplant	ARDS	Neg	Pos	Pos	Oseltamivir (Delayed)	Survived
45 M	Kidney transplant	Septic shock, abdominal pain, ARDS	Neg	Pos	Pos	Oseltamivir	Survived
69 F	COPD	ARDS	Pos	Pos	Pos	Oseltamivir	Survived
31 F	Hypothyroidism	ARDS	Neg	NS/Neg	Pos	Oseltamivir	Survived
36 F	Obesity	ARDS	Neg	Pos	Pos	Oseltamivir (Delayed)	Died

Characteristics of patients with H1N1 influenza A infection and respiratory failure.

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CHRONIC ALCOHOL INGESTION INCREASES EXPRESSION OF THE RECEPTOR FOR ADVANCED GLYCATION END (RAGE) PRODUCTS IN RAT ALVEOLAR MACROPHAGES

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Purpose of Study: Chronic alcohol abuse causes alveolar macrophage (AM) immune dysfunction and increases the frequency and severity of pneumonia. However, the mechanisms by which alcohol mediates its deleterious effects on the AM have not yet been fully elucidated. We hypothesized that chronic alcohol ingestion could impair AM immune function by altering the expression and/or function of the Receptor for Advanced Glycation End Products (RAGE). RAGE has both a membrane and a soluble isoforms that bind diverse ligands including advanced glycation end products. The membrane-bound isoform induces the release of pro-fibrotic and pro-inflammatory cytokines; however, the soluble isoform is thought to be protective by acting as a decoy receptor modulating the inflammatory response. Under normal physiologic conditions AM RAGE expression is low, but its expression during chronic alcohol ingestion has not been evaluated.

Methods Used: To test our hypothesis, we used western blot analysis to quantify the levels of soluble RAGE in lung lavage fluid from rats fed an isocaloric liquid diet $\pm$ alcohol for 12 or 20 weeks. In parallel, we examined total RAGE expression in alveolar macrophages isolated from these rats (western blot analysis cannot distinguish the membrane isoform from intracellular pools of the soluble isoform).

Summary of Results: The levels of soluble RAGE were significantly increased ($P<0.05$) in lung lavage fluid from both 12-wk and 20-wk alcohol-fed rats when compared to control-fed rats. In parallel, total RAGE protein levels were significantly increased ($P<0.05$) in AM from the alcohol-fed rats at both time points.

Conclusions: We conclude that chronic alcohol exposure induces RAGE expression in AM; whether or not this induction contributes to alcohol-induced immune suppression is as yet unknown but is being actively investigated in our laboratory. Currently we are extending these studies to determine if alveolar macrophages in RAGE knock-out mice are "protected" from alcohol-induced immune dysfunction. We speculate that alcohol-mediated RAGE expression has detrimental effects on AM immune function, possibly by interfering with normal regulation of the inflammatory response and thereby rendering individuals with alcohol use disorders susceptible to pneumonia and lung injury.

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MESENCHYMAL STEM CELLS MODULATE THE SYSTEMIC INFLAMMATORY RESPONSE TO ENDOTOXEMIA IN ALCOHOL-FED MICE

C. Co, D. Guidot, M. Rojas *Emory University, Decatur, GA.*

Purpose of Study: Alcohol abuse increases the risk of pneumonia and acute lung injury even in otherwise healthy individuals. In parallel, alcohol

can be toxic to the bone marrow and in severe cases can even cause pancytopenia. There is growing experimental evidence that bone marrow-derived mesenchymal stem cells (MSC) are part of the host response to acute lung inflammation where they appear to modulate inflammatory cytokine levels and facilitate lung repair. This suggests the possibility that alcohol-induced lung injury is exacerbated by an inadequate response by host MSC during acute inflammatory stresses. Therefore, in this study we hypothesized that infusion of exogenous MSC might attenuate acute inflammation in the experimental alcoholic lung during endotoxemia.

Methods Used: C57/Bl6 mice were given alcohol in their drinking water (20% w/v) for ≥ 8 weeks, and then acute lung inflammation was induced with intraperitoneal lipopolysaccharide (LPS; 1 mg/kg). Within 10 minutes of LPS injection, mouse bone marrow-derived MSC were infused intravenously (500,000 cells; provided by the Tulane Center for Gene Therapy) and mice were sacrificed 24hrs later. Serum was collected and the levels of multiple cytokines/chemokines were quantified using the Luminex platform. The pro-inflammatory cytokines/chemokines analyzed were: granulocyte colony stimulating factor (G-CSF), monocyte chemoattractant protein-1 (MCP-1), interleukin-6 (IL-6), interferon gamma inducible protein-10 (IP-10), and keratinocyte-derived chemokine (KC); in parallel, the anti-inflammatory cytokine interleukin-10 (IL-10) was determined.

Summary of Results: In these preliminary studies, MSC infusion appeared to modify the systemic inflammatory response in alcohol-fed mice as reflected by decreased serum levels of G-CSF, IL-6, IP-10, KC and MCP-1 24 hrs after the induction of endotoxemia, which paralleled a trend toward decreased IL-10 levels.

Conclusions: These studies suggest that an infusion of MSC appear to modulate the systemic inflammatory response to endotoxemia in alcohol-fed mice. If these effects prove to limit acute lung injury in an experimental model, it is possible that MSC infusions could be tested in alcoholic human subjects at high risk of acute lung injury because of pneumonia or sepsis.

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LONG TERM CIGARETTES SMOKE INDUCED HEMATOPOIETIC STEM CELLS DISFUNCTIONS BY PERTURBING NICHE FUNCTION

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Purpose of Study: Hematopoiesis occurs in unique microenvironments/ niches of bone marrow. Bone marrow niches maintain stem cells in a primitive state and control progenitor differentiation. Mesenchymal stem cells (MSCs) are believed to be a major component of the niche, supporting self-renewal, proliferation and differentiation of the hematopoietic stem cells (HSCs) through production of growth factors, cytokines and intercellular signals. Collectively the co-ordinate activities of the niches and the stem cells are responsible for regulating hematopoiesis in health and in response to infection. We hypothesized that chronic cigarette smoke exposure alters hematopoietic stems by inducing bone marrow stem cell niche dysfunction.

Methods Used: C57Bl/6 mice (female) were smoked 6 hours a day, 5 days / week for 6 months. Bone marrow cells were isolated and analyzed for HSCs and MSCs by flow cytometer (BD Bioscience). To determine niche function, 6 months smoked or control mice were irradiated with 8Gy, and transplanted with 106 whole bone marrows cells from 7 weeks old GFP-transgenic mice. Twenty weeks of post transplantation, eGFP positive bone marrow cells and peripheral blood cells were analyzed for HSC markers by Flow cytometer. Colony forming unit-fibroblast (CFU-F) assay was performed according to manufacturer protocol (Stem Cell Technology).

Summary of Results: Six-months of smoke significantly reduced the number of HSCs ($p<0.05$) and MSCs ($p<0.01$) cells in bone marrow. Engraftment of GFP+ bone marrow cells was adversely affected by smoking. Cigarette smoke reduced transplanted hematopoietic stem cells engraftment ($p<0.05$) and also reduced the number of myeloid progenitor cells ($p<0.05$) in the peripheral blood. CFU-F numbers were also significantly reduced ($p<0.05$) in smoked bone marrow cells.

Conclusions: Long-term cigarette smoke exposure reduces HSCs numbers in the bone marrow. Smoke-induced stem cell niche dysfunction is responsible, at least in part, for this defect. These findings help to explain abnormal host responses to infection in smokers.

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ESTROGEN REDUCES PANCREATIC INFLAMMATION PROCEEDING SEVERE BURNS IN RATSL. Farris, J. Gatson, D. Maass, J. Wigginton *University of Texas Southwestern Medical Center at Dallas, Dallas, TX.*

Purpose of Study: Multisystem and remote organ failure following burn injuries remains a significant cause of death each year. The mechanisms relating such organ failure to the burn injury are currently not fully understood. However, it is known that the systemic and remote effects of severe burns are at least in part driven by an increase in inflammation. This post-burn inflammatory response is regulated by certain factors which are released from the burn site; these factors include tumor necrosis factor- α (TNF- α), interleukin 1 β (IL-1 β), interleukin 10 (IL-10), and prostaglandins. In an effort to blunt the inflammatory response following injury, administration of estrogen in animal models has resulted in both decreased levels of circulating inflammatory cytokines and in various remote organs, as well as a decrease in mortality. Previous humans studies have demonstrated that pancreatic function is negatively affected following remote burn injuries. More specifically, a decrease in beta-cell function and an increase in plasma levels of IL-1 have been correlated with increased patient mortality. It is therefore hypothesized that administration of estrogen post-burn may protect the pancreas following remote burn injuries. The objective of this study is to elucidate the effect of acute estrogen treatment on IL-1 β , IL-6, IL-10 and TNF- α levels in the pancreas following severe burn injury.

Methods Used: In this study, male rats received 40% total body surface area burns. Fifteen minutes following burn, the animals received a subcutaneous injection of either placebo (corn oil) or 17 β -estradiol (0.5 mg/kg). The pancreas was harvested at various time points within the proceeding 24 hours, and then cytokine levels were measured using the ELISA method.

Summary of Results: Administration of estrogen significantly ($p < 0.05$) decreased the cytokine levels (IL-1 β , IL-6, IL-10, and TNF- α) in the pancreas compared to the placebo/burn group at multiple time points within twenty-four hours.

Conclusions: Following remote severe burn injury, single-dose estrogen significantly decreases the levels of inflammatory cytokines in the pancreas.

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INCREASED MATRIX METALLOPROTEINASE-9 AND -8 EARLY IN PEDIATRIC ACUTE RESPIRATORY DISTRESS SYNDROME PREDICTS LENGTH OF MECHANICAL VENTILATIONM. Kong, Y. Li, J. Clancy *University of Alabama at Birmingham, Birmingham, AL.*

Purpose of Study: Matrix metalloproteinase (MMP) -9 and -8 may play a key role in the modulation of neutrophil dominated lung inflammation seen in pediatric Acute Respiratory Distress Syndrome (ARDS). We aimed to undertake a comprehensive analysis of MMP activity in pediatric ARDS patients compared with non-ARDS pediatric controls.

Methods Used: Lung secretions were collected from 35 pediatric ARDS patients and 21 non-ARDS controls at 48 hours of intubation, and serially for those who remained intubated greater than 5 days in our Pediatric Intensive Care Unit (PICU). Samples were probed for MMP expression and activity using ELISA-based quantitative analysis.

Summary of Results: Total MMP-9 and -8 were elevated early in pediatric ARDS, with the greatest difference seen in active MMP-9 when compared to non-ARDS pediatric controls. Human Neutrophil Elastase (HNE) and myeloperoxidase (MPO) were up-regulated in ARDS subjects, and correlated positively with MMP-9 and -8, suggesting a common source from neutrophils. Higher MMP-9, MMP-9:TIMP-1 ratios and MMP-8 at 48 hours of ARDS onset and intubation predicted subjects who required a longer course of mechanical ventilation. Patients with the longest requirement for intubation demonstrated the highest MMP-9 activity and fraction of active MMP-9 at 48 hours, suggesting the role of MMP-9 dysregulation in ARDS pathology. In addition, the active fraction of MMP-9 increased with ARDS progression. Negative regulation was eventually restored, as the active fraction dropped in the late stage of protracted ARDS. HNE and MPO levels showed no clear relationship with the duration of mechanical ventilation in our ARDS subjects.

Conclusions: Our study confirms previous reports that MMP-9 and -8 are up-regulated in pediatric ARDS, and provides evidence that MMP-9 and MMP-

8 measurements early in the disease course help to predict the duration of ventilator support. MMP-9 activity and fraction of active MMP-9 at 48 hours of ARDS were most predictive of prolonged intubation. Together, these results lend support to the hypothesis that active MMP-9 and MMP-8 can serve as biomarkers to predict disease course in the pediatric ARDS population, and potentially identify targets to modify ARDS disease progression.

Renal, Electrolyte and Hypertension II**Concurrent Session**

1:00 PM

Saturday, February 27, 2010

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HYPOXIC REGULATION OF ERYTHROPOIETIN IN RENAL NON-UREMIC ANEMIAP. Kapitsinou^{1,2}, Q. Liu^{1,2}, T. Unger², J. Rha², O. Davidoff¹, CL. Erickson Miller³, V.H. Haase^{1,2} ¹Vanderbilt University Medical Center, Nashville, TN; ²University of Pennsylvania, Philadelphia, PA and ³GlaxoSmithKline, Collegeville, PA.

Purpose of Study: The kidney is the major physiologic source of erythropoietin (EPO) production in the adult. Studies in mice with global or liver specific HIF-2 deletion have shown that Hypoxia-Inducible Factor (HIF)-2 mediates the hypoxic induction of EPO. The goal of the current study is to investigate the role of renal HIF-2 specifically in the regulation of serum EPO and to examine the contribution of extrarenal tissue sources to the serum EPO pool in its absence.

Methods Used: We used Cre-loxP mediated recombination to ablate HIF-2 in the kidney, while HIF-2 mediated hypoxia responses in the liver remained intact. To characterize the hypoxic regulation of EPO, we exposed mutant and control mice to hypoxia and also pharmacological HIF stabilization.

Summary of Results: Mutant mice developed anemia with a mean Hematocrit (Hct) of 24% (± 0.6) compared to 46% (± 1.0) in controls ($n=26$ and 21; $P < 0.001$), while baseline serum EPO was reduced by 40%. Kidney function was preserved. Anemia was associated with HIF-1 stabilization in mutant kidneys and a 2.3-fold induction of HIF target gene Phd3 ($n=6$; $P < 0.01$), as determined by immunoblot and real time-PCR analysis respectively. Epo mRNA was down-regulated 50-fold in mutant kidneys compared to control ($n=6$, $P < 0.05$), whereas hepatic Epo mRNA was up-regulated ($n=6$, $P < 0.05$). Exposure to hypoxia, 10% O₂ for 10 days, increased Hcts in mutant and control mice to 41% ± 0.8 and 65% ± 3.6 respectively, while the increase in serum EPO was reduced by 50% in mutants. Hypoxic Epo induction in kidney was completely abolished in mutants, while hepatic Epo mRNA was increased 5.4-fold compared to normoxia ($n=4$; $P < 0.01$). Pharmacological HIF stabilization in mutants induced a significant increase in liver EPO production and was sufficient to correct their anemia.

Conclusions: Our data establish that HIF-2 mediates the hypoxic induction of EPO in the kidney and that the liver responds to hypoxia with a graded EPO response. We also show that the EPO producing ability of the liver could be exploited therapeutically, when the kidney, the main source of EPO, fails.

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HIGH SALT DIET UP-REGULATES COLLECTING DUCT RENIN AND EXACERBATES HYPERTENSION, PROTEINURIA, AND ANGIOTENSIN II (ANGII) URINARY EXCRETION IN CHRONIC ANG II-INFUSED RATSM. McCormack¹, L. Navar^{1,2}, MC. Prieto^{1,2,3} ¹Tulane University, Sch of Med, New Orleans, LA; ²Tulane University, New Orleans, LA and ³Tulane University, New Orleans, LA.

Purpose of Study: High salt (HS) intake inhibits both the systemic and intrarenal renin-angiotensin system; however, when AngII is not suppressed, HS exacerbates hypertension and renal injury. This study examined the effects of HS on the magnitude of the hypertension, renin gene expression in renal medulla (CD), and urinary excretion of AngII during AT1 receptor antagonism with candesartan (Cand) in chronic AngII-infused rats.

Methods Used: Sprague-Dawley rats ($n=24$) chronically AngII-infused (80 ng/min, SC via minipumps; for 14 day) were distributed into 5 groups: 1) normal salt diet (NS); 2) high salt diet (HS, 8% NaCl); 3) AngII; 4) Ang II+HS; and 5) AngII+HS+Cand (25 mg/L, drinking water). Systolic blood

pressures (SBP) were measured by tail cuff; 24-h urine was collected for determinations of AngII excretion; and kidneys harvested for CD renin gene expression by Western blot and qRT-PCR.

Summary of Results: HS alone did not change basal SBP (128 ± 7 vs. 123 ± 6 mmHg); however, the increase in SBP was exacerbated when HS was combined with AngII (AngII: 178 vs. AngII+HS: 222 mmHg). Proteinuria was present with HS alone and was further augmented in AngII+HS rats (NS: 5 ± 1 ; HS: 36 ± 13 ; AngII: 39 ± 5 ; Ang II+HS: 128 ± 8 mg/day). HS diet did not inhibit renin in distal nephron segments nor did it exert any further effects on the up-regulated CD renin levels observed in AngII infused rats. By day 13, urinary excretion of AngII increased in AngII and Ang II+HS rats, and went back to normal in rats treated with Cand. Also, candesartan attenuated the AngII-dependent increases in SBP and proteinuria, as well as prevented the up-regulation of CD renin in renal medull of AngII+HS rats.

Conclusions: These findings demonstrate that HS intake leads to proteinuria independently of increases in SBP and that; it exacerbates hypertension and proteinuria in chronic AngII-infused rats. Inappropriate up-regulation of renin in the collecting ducts of rats fed a HS diet may contribute to increase intrarenal AngII formation as indicated by the increases in urinary AngII, thus exacerbating the hypertension and renal injury during AngII-dependent hypertension.

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CHRONIC BLOCKADE OF ENDOGENOUS FORMATION OF HYDROGEN SULFIDE CAUSED INCREASE IN SYSTEMIC BLOOD PRESSURE IN RATS

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Purpose of Study: Hydrogen sulfide (H₂S) is produced endogenously from L-cysteine by the action of the enzymes cystathionine γ -lyase (CSE) and cystathionine β -synthase (CBS). The roles of these enzymes in the regulation of systemic blood pressure (SBP) are not yet clearly defined. In the present study, we have examined the effect of chronic deficiency of endogenous H₂S induced by inhibitors of CSE and CBS on SBP and renal parameters in rats.

Methods Used: Sprague-Dawley rats were chronically treated with inhibitors of CSE (DL-propargylglycine, PAG; 37.5 mg/kg/day i.p.) and CBS (aminooxyacetic acid, AOA; 8.75 mg/kg/day i.p.) either singly or in combination. Before the start, and then once in every week during treatment period, SBP was measured by tail-cuff plethysmography and 24hr urine collection was taken using metabolic cages. Concentrations of sodium and H₂S in urine were measured using flame photometry and colorimetry, respectively.

Summary of Results: After three week period of drug treatments, only the group with combination therapy showed significant decrease in urinary excretion of H₂S (UH₂SV) and an increase in mean SBP. There were also increase in urine flow (V) and sodium excretion (UNaV) in this group with combination treatment, which were probably due to consequent pressure dependent effects on renal excretory function. The findings from the 3 week period of treatment are summarized in the following Table.

Conclusions: The findings indicate that the effect of CSE inhibition alone is counteracted by the activity of CBS, and vice versa, in maintaining the H₂S level endogenously. These data demonstrate that the deficiency in endogenous H₂S production leads to an increase in SBP and suggest that this hypertensive response to H₂S deficiency is mostly related to its direct effects of an increase in vascular tone, rather to its possible effects on renal excretory function.

Treatment groups	SBP (mmHg)	V (mL/24hr)	UNaV (mmol/24hr)	UH ₂ SV (nmol/24hr)
Vehicle control (n=6)	103 ± 5.0	17 ± 2.0	5.0 ± 1.0	560 ± 101
PAG (n=6)	106 ± 3.0	26 ± 1.0	8.0 ± 2.0	524 ± 55
AOA (n=6)	99 ± 3.0	17 ± 2.0	5.2 ± 1.0	619 ± 85
AOA+PAG (n=6)	$129 \pm 1.3^*$	$42 \pm 3.0^*$	$18.4 \pm 3.0^*$	$208 \pm 26^*$

*, $P < 0.05$ vs. values in all other treatment groups.

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MARINOBUFAGENIN INDUCES IN VIVO AND IN VITRO GADD45a STRESS SIGNALING

MN. Uddin, D. Horvat, S. DeMorrow, E. Agunanne, B. Kumar, JB. Puschett *Texas A & M University College of Medicine/Scott & White, Temple, TX.*

Purpose of Study: Preeclampsia (PE) is a hypertensive disorder unique to pregnancy. Marinobufagenin (MBG) is an endogenous mammalian cardiotonic steroid that is increased in PE. Placental stresses including hypoxia, ischemia and an increase in sfms-like tyrosine kinase-1 (sFlt-1) are important in the etiopathogenesis of PE. The Gadd45a stress sensor protein is an upstream modulator of pathophysiological changes observed in PE. The aim of our study was to elucidate the role of MBG in Gadd45a stress signaling.

Methods Used: Placental samples from the following groups of rats were studied: normal pregnant (NP, n = 8); pregnant rats which received weekly injections of desoxycorticosterone acetate and 0.9% saline as their drinking water (PDS, n = 9); normal pregnant rats injected with MBG (NPM, n = 8); and PDS rats injected with resibufogenin (RBG), (PDSR, n = 8). In addition, human first trimester extravillous cytotrophoblast (CTB) cells were treated with various concentrations of MBG (0.1, 1, 10 or 100 nM) in vitro. Gadd45a expression was measured by immunoblotting. The MBG-induced effect on cell cycle arrest was determined by FACS analysis. sFlt-1 and caspase 3 and 8 activities in the placental homogenates and in the MBG-induced CTB cells were measured by EIA.

Summary of Results: Placental Gadd45a expression, sFlt-1 concentrations, and caspase 3 and 8 activities were significantly higher in PDS and NPM compared to NP and PDSR rats. In CTB cells, MBG (1, 10 or 100 nM) significantly arrested progression of the cell cycle compared to DMSO-treated cells, whereas 0.1 nM MBG had no effect. There was a significantly higher percentage (~80%) of cells in the G0/G1 phase in the MBG 1, 10 and 100 nM-treated cells compared to basal and to 0.1 nM treated cells (~55%). Gadd45a protein was significantly upregulated in the 1, 10 and 100 nM MBG-treated cells compared to basal. MBG (1, 10 and 100 nM) also significantly induced the secretion of sFlt-1 in the cell culture media.

Conclusions: 1) Gadd45a expression, apoptotic signaling, and sFlt-1 secretion are upregulated in the placenta of PDS and NPM rats; 2) MBG is involved in the causation of these alterations 3) RBG prevents these changes. 4) MBG causes cell cycle progression arrest, upregulates Gadd45a expression, and induces secretion of sFlt-1 in CTB cells.

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RESIBUFOGENIN PREVENTS ANGIOGENIC IMBALANCE IN A RAT MODEL OF PREECLAMPSIA

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Purpose of Study: Preeclampsia (PE) may result from an imbalance between pro-angiogenic and anti-angiogenic factors. We studied these factors in our rat model of PE in which marinobufagenin (MBG, a bufodienolide) plays an important role.

Methods Used: Animals were grouped into: normal, non-pregnant (C, n = 9); normal pregnant (NP, n = 10); NP injected weekly with DOCA intraperitoneally (IP) and whose drinking water was replaced with 0.9% saline (PDS, n = 8); NP given daily injections of MBG (0.765 μ g/100g) once pregnancy was established (NPM, n = 7); PDS given daily injections of resibufogenin [RBG, an antagonist

Angiogenic factors in day 17– 20 of pregnancy

Animal Group	sFlt-1 A (pg/ml) Ψ Flt-1 B (ng/g tissue) Φ Ω	Ratio : sFlt-1 /PIGF A Ψ λ Ratio : sFlt-1 /PIGF B Φ Ω	PIGF A (pg/ml) Ψ λ PIGF B (ng/g tissue) Φ	VEGF A (pg/ml) Σ VEGF B (ng/g tissue) χ	sEng A (pg/ml) Ψ Eng B (ng/g tissue)	TGF- β A (ng/ml) Ψ TGF- β B (ng/g tissue)
C	386 ± 25 A	27 ± 2 A	14 ± 1 A	18 ± 1 A	220 ± 18 A	6.2 ± 0.6 A
NP	2778 ± 52 A 55 ± 4 B	105 ± 3 A 0.5 ± 0.1 B	26 ± 2 A 104 ± 10 B	29 ± 2 A 17 ± 2 B	821 ± 22 A 6.2 ± 0.3 B	4.3 ± 0.7 A 0.6 ± 0.1 B
PDS	2781 ± 30 A 73 ± 6 B	154 ± 13 A 1.1 ± 0.1 B	18 ± 2 A 72 ± 10 B	20 ± 1 A 19 ± 2 B	830 ± 25 A 6.1 ± 0.2 B	4.1 ± 0.4 A 0.6 ± 0.2 B
NPM	2748 ± 41 A 140 ± 20 B	164 ± 12 A 2.1 ± 0.6 B	16 ± 1 A 68 ± 12 B	19 ± 2 A 11 ± 2 B	822 ± 13 A 6.0 ± 0.1 B	4.1 ± 0.3 A 0.6 ± 0.1 B
PDSR	2749 ± 32 A 52 ± 5 B	108 ± 4 A 0.5 ± 0.1 B	25 ± 1 A 97 ± 10 B	28 ± 2 A 13 ± 2 B	830 ± 13 A 6.0 ± 0.2 B	3.9 ± 0.4 A 0.6 ± 0.1 B

Symbols and statistical analyses: A = Plasma level Ψ $p < 0.05$; C vs NP, PDS, NPM and PDSR λ $p < 0.05$; NP and PDSR vs PDS and NPM Σ $p < 0.05$; NP and PDSR vs C, PDS and NPM B= Placenta level Φ $p < 0.05$; NP and PDSR vs PDS and NPM χ $p < 0.05$; NP and PDS vs NPM and PDSR Ω $p < 0.05$; PDS vs NPM.

TABLE 2. Number of pups, BP levels and proteinuria.

Animal group	Pup count	Baseline BP(mm Hg)	Final BP(mm Hg)	Protein uria (mg/24hr)
Control		104 ± 5	102 ± 4 λ	1.1 ± 0.9 λ
NP	15.0 ± 1.9	105 ± 4	90 ± 6 Ω	2.4 ± 1.2
PDS	11.1 ± 1.4 Φ	103 ± 7	140 ± 8 Φ Ω	5.6 ± 1.8 Φ
PDSR	14.7 ± 1.3	106 ± 6	87 ± 5 Ω	2.5 ± 1.1
NPM	12.2 ± 1.7 Φ	108 ± 7	132 ± 6 Φ Ω	4.8 ± 1.6 Φ

Symbols and statistical analyses: Φ p <0.05 NP and PDSR vs PDS λ p <0.05 C vs NP, PDS, PDSR and NPM Ω p <0.05 Baseline vs Final.

of MBG (30 μg/kg/day)] IP from day 4 of pregnancy (PDSR, n = 8). The angiogenic factors were measured on days 17-20 of pregnancy.

Summary of Results: There was evidence of angiogenic imbalance in the “preeclamptic” PDS animals (Tables 1 & 2). RBG prevented these abnormalities.

Conclusions: Angiogenic imbalance contributes to the pathogenesis of the preeclamptic syndrome in our rat model. MBG plays a role. RBG prevents the syndrome as evidenced by normal BP, proteinuria and pup count in the PDSR rats.

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ENVIRONMENTAL TOBACCO SMOKE: ROLE IN PROGRESSION OF DIABETIC NEPHROPATHY

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Purpose of Study: Clinical studies suggest that smoking is a risk factor in the progression of chronic kidney disease, including diabetic nephropathy. The mechanisms involved, however, are not completely understood. We have previously demonstrated that nicotine, one of the compounds present in large amounts in tobacco smoke, promotes mesangial cell proliferation and fibronectin production. In this study, we hypothesized that exposure to environmental tobacco smoke (ETS) promotes the progression of diabetic nephropathy by increasing the expression of cytokines such as TGF-β, resulting in increased mesangial expansion and matrix deposition.

Methods Used: Eight-week-old diabetic (db/db) mice were divided into two groups. The experimental group (n=12) was exposed to ETS at a concentration of 30 mg/m³ for 6 hrs/day, 5 days/week for eight weeks. The control group (n=8) was not exposed to smoke. Urine was collected before euthanasia for albumin (ELISA) and creatinine measurements (mass spectrometry). After euthanasia, the kidneys were harvested for morphometric analysis and molecular biology (Western blot). Serum was saved for cotinine measurements (ELISA).

Summary of Results: As shown in the table, ETS exposure resulted in significant mesangial expansion that was accompanied by concomitant increases in TGF-β and fibronectin expression. There was, however, no difference in albumin urinary excretion between the two groups. Serum levels of cotinine found in the ETS group were similar to those found in smokers.

Conclusions: In diabetic mice, exposure to ETS worsens the severity of diabetic nephropathy, as assessed by mesangial expansion and extracellular matrix production. Increases in TGF-β suggest that this cytokine is implicated as a mediator of these effects. These studies unveil mechanisms that could explain the deleterious effects of smoking in the progression of diabetic nephropathy.

	Control (n=8)	ETS (n=12)
Mesangial Area (μm ²)	11134 ± 887.13	18131 ± 2274.5*
Glomerular Area (μm ²)	80452 ± 1963.4	69577 ± 8707.1
Mes/Glom Ratio	0.1382 ± 0.0098	0.2556 ± 0.0081*
Fibronectin WB (OD Units)	0.6376 ± 0.0120	0.7833 ± 0.0358*
TGF-β WB (OD Units)	0.6934 ± 0.0907	0.8852 ± 0.0538*
Urinary Albumin/Creatinine (mg/mmol)	0.1161 ± 0.0180	0.1179 ± 0.0147
Plasma Cotinine (ng/mL)	Undetectable	80.591 ± 7.4533*

*P < 0.05 vs. control.

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ENHANCED URINARY ANGIOTENSINOGEN EXCRETION IN CYP1A1-REN2 TRANSGENIC RATS WITH INDUCIBLE ANG II-DEPENDENT MALIGNANT HYPERTENSION

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Purpose of Study: Previous studies have demonstrated that ANG II-infusion in normal rats results in paradoxical increases in renal expression of angiotensinogen mRNA and protein. In addition, the urinary excretion of angiotensinogen is significantly increased in ANG II-infused hypertensive rats, which is associated with an augmentation of intrarenal ANG II levels. These findings suggest that urinary angiotensinogen excretion rates provide an index of intrarenal ANG II levels in ANG II-dependent hypertensive states. However, little information is available regarding the urinary excretion of angiotensinogen in ANG II-dependent malignant hypertension. The present study was performed to determine if urinary angiotensinogen excretion is increased in Cyp1a1-Ren2 transgenic rats [strain name: TGR (Cyp1a1Ren2)] with inducible ANG II-dependent malignant hypertension.

Methods Used: Adult male Cyp1a1-Ren2 rats (n=6) were fed a normal diet containing 0.3% indole-3-carbinol (I3C) for 10 days to induce ANG II-dependent malignant hypertension.

Summary of Results: Rats induced with I3C exhibited pronounced increases in systolic blood pressure (SBP) (208±7 vs. 127±3 mmHg, P<0.001), marked proteinuria (29.4±3.6 vs. 5.0±0.4 mg/day, P<0.01), and augmented urinary angiotensinogen excretion (996±186 vs. 199±19 mg/day, P<0.05). Chronic administration of the AT1 receptor antagonist, candesartan (25 mg/L in drinking water, n=6), prevented the I3C-induced increases in SBP (125±5, P<0.001), proteinuria (7.3±1.5 mg/day, p<0.001) and urinary angiotensinogen excretion (488±51 mg/day, P<0.05).

Conclusions: The present findings confirm that AT1 receptor activation contributes to the increase in SBP and proteinuria in Cyp1a1-Ren2 transgenic rats with ANG II-dependent malignant hypertension. These data also demonstrate that the urinary excretion of angiotensinogen is markedly augmented in ANG II-dependent malignant hypertension. Such increased urinary angiotensinogen excretion likely reflects an AT1 receptor-mediated stimulation of intrarenal angiotensinogen production which may contribute to augmented intrarenal ANG II levels and, thereby, to the increased blood pressure in Cyp1a1-Ren2 transgenic rats with inducible ANG II-dependent malignant hypertension.

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ACUTE KIDNEY INJURY (AKI) IN CANCER PATIENTS: INCIDENCE, RISK FACTORS AND OUTCOMES

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Purpose of Study: AKI appears to be on the rise in the cancer population, but its incidence, risk factors or influence on patient-outcomes is not known.

Methods Used: Electronic patient records were prospectively collected in 5491 patients hospitalized to UT MD Anderson Cancer Center for 3 months between May 1, 2006 and July 31, 2006. For each patient demographic information and laboratory and pharmacy data were obtained. Descriptive, survival and logistic regression analyses were performed.

Summary of Results: The incidence of AKI defined as an absolute increase in serum creatinine ≥ 0.3 mg/dl was 28% among the 5013 patients. Preexisting AKI was noted in 14% patients admitted to hospital where as 14% patients acquired AKI in the hospital. The mean (±SD) age was 54±18 y and men were 52%. In univariate analysis, frequency of AKI was significantly higher in patients on chemotherapeutic, anti-diabetic and antibiotic medications. Patients admitted to ICU were 50% more likely to develop AKI. AKI in cancer patients was found to be associated with 1) A high blood sugar of over 200 mg/dl (p<0.001), 2) Admission through Emergency Center or admission to ICU (p<0.001), and 3) Admission Services Group or cancer types (p=0.001), for example, admission to Stem Cell Transplant Department or hematological malignancy. Patient with AKI had a mortality rate of 15% compared to patients without AKI who had mortality rate of only 2.3 (p<0.001). In multivariate regression analysis, patient who had AKI had higher rates of hospital stay (OR 2.1, CI: 1.7-2.6; P<0.0001) and mortality (OR 6.0, CI: 4.3-8.2; P<0.0001).

Conclusions: 1) the AKI incidence rate of 28% among patients admitted to cancer hospital is higher than the rate known for patients admitted to a community hospital, 2) the risk factors for AKI include diabetes, type of cancer and cancer therapy and 3) both mortality and hospital stay are adversely affected by the development of AKI in hospitalized cancer patients.

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TUBULAR INJURY-BASED BIOMARKERS PREDICT TOXIC-ACUTE KIDNEY INJURY (AKI) PRIOR TO THE RISE IN SERUM CREATININE IN A CISPLATIN-INDUCED AKI MODEL: COMPARATIVE ANALYSIS OF KIDNEY INJURY MOLECULE-1, NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN, AND N-ACETYL-GLUCOSAMINIDASE

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Purpose of Study: Although studies have suggested a number of tubular injury-based biomarkers to predict AKI earlier than traditional biomarkers such as serum creatinine, few have directly compared the prominent new markers in animal or clinical settings.

Methods Used: This study aimed at analyzing KIM-1, NGAL and NAG in a cisplatin-induced AKI model. Groups of male Sprague Dawley rats (350 g) injected with cisplatin (n=6) at 6 mg/kg of body weight once through their tail veins, along with saline injected controls (n=4) were euthanized at 2, 4, 12 and 24h, and on days 2, 3, 6 and 10; and urine, blood, and kidney samples were collected.

Summary of Results: A significant increase in serum creatinine was noted only on day 3 (1.42 0.16 mg/dl vs. 0.30 0.04 mg/dl; mean SE; P<0.05). Urinary NAG levels corrected for urine creatinine, were elevated as early as 2h (0.006 0.002 unit/mg vs. 0.004 0.001 unit/mg creatinine; P<0.05) remaining significantly elevated through day 6. Both urine NGAL and KIM-1 levels, measured by using Luminex-based multiplex assays, were elevated within 2h after injection (NGAL: 4.23 1.37 ng/mg vs. 2.57 0.60 ng/mg; KIM-1: 0.032 0.018 ng/mg vs. 0.008 0.003 ng/mg creatinine) but did not reach statistical significance. All three biomarkers were significantly elevated on day 3 (NAG: 0.009 0.001 unit/mg vs. 0.002 0.001 unit/mg; NGAL: 7.48 2.08 ng/mg vs. 2.25 0.05 ng/mg; KIM-1: 0.165 0.068 ng/mg vs. 0.078 0.048 ng/mg creatinine). The levels decreased during day 6 and the difference was no longer significant on day 10. The area under the curve was: urinary NAG > NGAL > KIM-1.

Conclusions: Thus, we find in our study that urinary tubular injury-based proteins, particularly NAG levels, were elevated as early as 2h after cisplatin injection (compared with 3 days for serum creatinine) and remained elevated up to 6 days. These biomarkers can detect AKI early facilitating early intervention, which might alter the course of AKI and patient outcomes thus raising the need for similar clinical studies in human AKI settings.

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THE PRIMARY CILIUM IS REQUIRED FOR VASOPRESSIN MEDIATED AQUAPORIN-2 TRAFFICKING

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Purpose of Study: In polycystic kidney disease (PKD), proteins necessary for salt and water balance e.g., Na/K ATPase are mislocalized. Recently, the primary cilium has been linked to PKD. Thus, the purpose of this study is to determine the role of the primary cilium in vasopressin mediated Aquaporin 2 (AQP2) trafficking and fluid absorption.

Methods Used: In this study we used PCDNA (cilia -) and BAP2 (cilia +/rescue) cell lines from a PKD mouse model (orpk mouse). In our localization studies, confluent and differentiated cells on impermeable or permeable supports were probed for AQP2 and vasopressin 2 receptor (V2R) by indirect immunofluorescence using a confocal laser microscope. Differential interference contrast imaging was used to visualize cell morphology changes after drug treatment. For membrane fractionation and protein analysis, we used biotinylation and Western Blot analysis, respectively.

Summary of Results: PCDNA cells grown on an impermeable support formed domes after 30 minutes of apical 10nM vasopressin treatment, while BAP2 cells did not. We found that AQP2 localized to the subapical compartment and partially at the basolateral membrane. However, 12 hour vasopressin treatment increased AQP2 expression at the apical and

basolateral membrane in PCDNA cells but not in controls. V2R localized mainly to the basolateral membranes but no observable changes were detected after stimulation in each cell lines. Analysis of each cell lines apical membrane fractions showed AQP2 in equal levels before stimulation, whereas in PCDNA cells the glycosylated form of AQP2 was elevated in apical membranes fractions compared to controls.

Conclusions: In summary, V2R mediated water absorption through AQP2 in cilia (-) PCDNA cells, as indicated by water filled domes at the basolateral membrane, suggests mislocalized V2R to the apical membrane. Furthermore, basolateral vasopressin treatment triggers the insertion of AQP2 into the apical and basolateral membranes in PCDNA cells grown on permeable supports. The large increase in AQP2 into the basolateral membrane may account for the fluid accumulation beneath the cells causing the observed dome formations. Thus, the primary cilium appears to be required for normal trafficking of AQP2 and V2R signaling events.

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A SINGLE CENTER'S EXPERIENCE SUPPORTS UNOS POLICY CHANGE IN ALLOCATING HLA-MATCHED KIDNEYS

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Purpose of Study: The effect of HLA match on renal graft survival has become controversial, so is the UNOS mandatory sharing policy. In order to answer the question of whether the recent change in policy would be supported by a single center's data in the era of modern immunosuppressive regimen, we retrospectively compared the outcomes of HLA-matched and HLA-mismatched kidney transplants performed from January 1997 to December 2007 in our center.

Methods Used: Based on the 6 antigens at HLA-A, B, and DR loci, living and cadaveric donor kidney transplants were divided into two groups: 1) HLA matched (M) group that included HLA identical, phenotypically matched and zero mismatched kidneys, and 2) HLA-mismatched (MM) group that represented no match at any of the 6 HLA antigens. Cadaveric donor kidney transplants were further subgrouped into those with panel reactive antibody (PRA) > 20% and < 20%. Tacrolimus, mycophenolic acid and steroids were used as maintenance therapy and basiliximab induction was added for MM group.

Summary of Results: A total of 229 kidney transplants were included with median follow-up of 5.1 years. The 5-year death-censored graft survival by Kaplan-Meier method was significantly higher in M group than in MM group for cadaver kidney transplants (log rank p = 0.018). The graft survival advantage was detected in sensitized patients with PRA > 20% (p = 0.023), but not in those with PRA < 20% (p = 0.32). The graft survival was not statistically different between the M and MM groups for living donor kidney transplants (p = 0.077). HLA mismatch was an independent risk for graft loss (HR 2.27, 95% CI 1.009-5.09, p = 0.047) and acute rejection was a significant cause of graft loss in the mismatched cadaveric donor kidney transplants (p = 0.035).

Conclusions: With the modern immunosuppressive regimen, the survival advantage of HLA matched kidneys is limited to cadaveric kidney transplants in the sensitized patients with PRA > 20%. Our data support the policy change of mandatory sharing of HLA matched kidneys to sensitized patients only. Acute rejection remains a significant cause of graft loss in HLA-6-antigen mismatched cadaver kidney transplants, for whom more potent induction therapy should be considered.

Southern Society of General Internal Medicine Research Abstract Session A

8:30 AM

Friday, February 26, 2010

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DOES INTERNET ADVERTISEMENT INCREASE TRAFFIC IN A CME WEB-BASED CULTURAL COMPETENCY CURRICULUM?

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Purpose of Study: Online continuous medical education (CME) activities are ubiquitous; however, optimal strategies to increase utilization are not well determined. We explored the impact of an advertisement strategy on utilization of an online cultural competency curriculum.

Methods Used: We tracked visits to an open access cultural competency curriculum for four consecutive 8-week periods in 2009. We designed and purchased Internet advertisement using Google Ads® to display cultural or hypertension related ads. Following a Google® algorithm, ads appeared on the right side of the screen after any user typed any of the selected phrases. Ads were only displayed during the second (cultural) and fourth (hypertension) 8-week periods; the first and third 8-week periods served as controls. We compared logged CME activity between periods, user type, and day of the week.

Summary of Results: During the 32 weeks, 88 users registered, 59% of whom were practicing physicians. We observed no differences in the mean number of users logged by period, control 1 (mean 1.1, SD 0.3), cultural ad (1.4, 0.7), control 2 (1.9, 1.5), and hypertension ad (1.5, 0.9) ($p=0.16$); we also did not observe any differences when grouped by control vs. any advertisement (1.3, SD 0.8; 1.4, SD 0.8; respectively) ($p=0.44$). Practicing physicians logged in more frequently (mean 1.5; SD 0.9) as compared to trainees or others (1.1; SD 0.4) ($p=0.02$). We observed no differences between day of the week logged in and user type (practicing physician or not); $p=0.10$. The days of the week more frequently observed were Monday (17%), Wednesday (16%), Thursday (25%), and Friday (17%); followed by Sunday (13%), Tuesday (8%), and Saturday (4%).

Conclusions: An Internet advertisement strategy did not change utilization of a Web-based CME cultural competency curriculum. Future studies should identify best strategies to increase utilization and guide recruitment efforts in online continuous medical education activities.

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DOES PATIENT SELF-PERCEIVED COMPLEXITY AFFECT SATISFACTION WITH CARE?

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Purpose of Study: Little is known about patient self-reported complexity. We hypothesize that patients' complexity ratings will predict their satisfaction and a difference in complexity ratings between residents and patients will be inversely related to patient satisfaction.

Methods Used: During a summer period, research assistants observed internal medicine team rounds and recorded the teams' activities, census, and time devoted to each patient. Residents were asked to complete a patient complexity instrument on a 10-point, Likert-type scale (1=not complex, 10=very complex). An anonymous survey instrument was administered to consented patients assessing patient satisfaction on a 5-point scale as well as their perceived level of medical complexity (1-10). Descriptive statistics, Pearson and Spearman correlations, and multiple regression were analyzed with SAS 9.1.

Summary of Results: Fifty-four patient survey instruments were collected. Of these, 41 had corresponding resident complexity ratings. The mean patient complexity rating was greater than the mean resident score (6.60 and 4.97, $p=.0007$) and the mean patient satisfaction rating was 4.4. Whereas resident complexity rating was shown to correlate with patient satisfaction ($r=.32$ $p=.04$), patient complexity rating was not ($p=.39$). The simple difference between the two ratings also was not predictive ($p=.42$). Because the overall mean satisfaction was high, complexity and satisfaction means were categorized to examine effect size beyond the simple correlation. When residents and patients agreed to a high level of complexity, 70% of patients gave the highest rating on satisfaction. Other combinations of resident and patient perceptions of complexity yielded only a 23% top approval rating showing a significant effect ($p<.05$).

Conclusions: Although patient perception of the complexity of their medical conditions does not independently correlate with their inpatient satisfaction, it appears to play a role when there is either significant agreement or disagreement with the residents' perceptions. Future research could investigate what contributes to patient and resident perceptions of complexity, especially in the context of predicting patient satisfaction with their medical care.

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PRACTICE MATTERS: RELATIONSHIP BETWEEN PREPARATION STYLE AND CHANGES MADE TO SCIENTIFIC PRESENTATIONS

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Purpose of Study: Presenters at scientific meetings utilize a variety of preparation methods for their oral presentations. In data reported elsewhere, we have shown that the majority of presenters practice prior to presenting at a scientific meeting. Most presenters prepare by practicing alone, however slide review by a mentor, and practice in front of a group of more experienced colleagues were perceived as more useful. We sought to describe the different changes made in light of the various preparation styles.

Methods Used: Oral presenters at three academic general internal medicine meetings were invited by e-mail to complete an 11-item web based survey (2008–2009). We asked: 1) the frequency and settings of preparation prior to the presentation; 2) the changes presenters made in response to feedback; and 3) the perceived utility of practice and feedback on the presentation (Likert scale 1= very detrimental to 5= very useful). Changes were grouped by content (focus, objectives, and conclusions), visual aids (font/text, number of words, slide background, graphics, and animation), and delivery style (mannerisms).

Summary of Results: Of the 279 presenters, 182 responded (65% response rate). Presenters made a mean of 2.4 (SD 1.7) different types of changes to their presentations during preparation. 69% made changes to visual aids, 49% changed presentation content, and 26% changed their delivery style. Practicing alone was not associated with any specific type of change, while slide review and presenting to a group resulted in changes to both visual aids and content (all $p<0.001$).

81% of responders reported that practice and feedback were useful or very useful to their preparation. Responders who employed the practice alone, slide review, or practice in front of a group preparation styles each reported higher utility of practice than those who did not ($p=0.003$ for practice alone, $p<0.001$ for slide review and practice in front of a group).

Conclusions: Presenters benefited from practicing their presentation and obtaining feedback in a variety of settings. Presenters were more likely to make changes in response to slide review by a mentor and practicing in front of a group. Mentors and colleagues provide important input to the process of presentation preparation.

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ATTITUDES OF RESIDENTS, PATIENTS AND CAREGIVERS TO HOUSE CALLS: BETTER THAN SLICED BREAD?

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Purpose of Study: House calls are an important form of medical care and provide vital experience for physician training. Some programs have instituted house calls in their training but little is known about patients and caregivers reactions to having their physician see them in their homes. House calls add an important dimension to residents' knowledge of patients and their environments and offer an additional setting in which to develop the physician/patient relationship. To achieve the above and foster patient connectedness and humanism training we instituted a house call program. We explored the reaction of patients and caregivers to the house call experience.

Methods Used: One half day each week a team of 1 faculty, 2 residents, and a nurse do house calls for 2 patients. Qualitative and quantitative data are gathered from patients, caregivers and residents. Phone surveys are administered to the patient and primary caregiver within one week of the visit regarding reactions to visit, knowledge of personal medical conditions, understanding of proper medical care and safety guidelines and opened questions regarding what was learned from the visit, suggestions for different approaches and general comments.

Summary of Results: Preliminary survey data were gathered from 29 patients and 24 caregivers. 72% patients reported positive learning of their medical conditions. Quantitative and qualitative responses indicated improved ability to communicate with their physician. Specific patient and caregiver learning outcomes related to optimization of patient care were identified. Data from residents indicated overwhelmingly positive reactions to housecall and receptivity to continuing housecalls in the future.

Conclusions: Preliminary results suggest that patients, caregivers, and physicians have positive experiences with home visits. Patient, caregiver, and medical professional education can occur effectively within a housecall modality. These preliminary data provide support for continued efforts to incorporate home visits as part of residency training to enhance the physician role in patient and caregiver education, enhance physician/patient relationship and improve communication between the physician, patient and caregiver.

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USING VOXEL-BASED MORPHOMETRY TO UNDERSTAND THE STRUCTURAL PROGRESSION OF ALZHEIMER'S DISEASE

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Purpose of Study: The application of Voxel-Based Morphometry to MRI scans of Alzheimer's disease (AD), Mild Cognitive Impairment (MCI), and normal control (NC) patients allow the regional brain volume differences among these cohorts to be identified and compared to understand the progression of AD.

Methods Used: T1 MPRAGEs were obtained from the University of Texas-Southwestern AD Database and each patient, without any complicating factors, was placed in a cohort that was matched for size, age, and gender. The MPRAGE data was analyzed using the SPM5 software package along with Matlab 7.4 R2007a. After normalization to the SPM5 T1 Template, the normalized image was segmented into separate gray and white matter images. The gray matter image was then smoothed at an 8 mm kernel so that two sample t-tests can be applied for comparison. The two-sample t-test between NC and AD was run at a relative threshold of 0.2, a p-value of 0.03, and a minimum cluster size of 50 voxels. The two-sample t-test between NC and MCI was run at a relative threshold of 0.2, a p-value of 0.05, and a minimum cluster size of 50 voxels.

Summary of Results: The comparison between NC and AD patients show six areas of decreased gray matter volume in the AD patients relative to NC. These areas were located approximately in the left hippocampus, right hippocampus, left parahippocampal gyrus, right parahippocampal gyrus, left lateral temporal lobe, and the left insula. The comparison between NC patients and MCI patients show four areas of decreased gray matter volume in the MCI patients relative to NC. These areas were located approximately in the superior left hippocampus, superior right hippocampus, left putamen, and left lateral temporal lobe.

Conclusions: The finding that the areas with decreased gray matter volume are in regions associated with memory is consistent with the dementia found with AD and the slight dementia found in MCI. Since amnesic MCI patients often progress to full AD over time, MCI is often seen as a very early stage of AD and a comparison between the overlays of MCI patients to AD patients can be used to study the progression of AD. Such a comparison shows that AD starts in the superior right and left hippocampus and progresses throughout the rest of the hippocampus and associated parahippocampal gyri and then throughout the medial, temporal, and lateral lobes.

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INTEGRATING MENTAL HEALTH AND PRIMARY CARE IN A PATIENT-CENTERED MEDICAL HOME

D. Dunn, C. Wilson, B. Springgate, E. Price-Haywood *Tulane University Health Sciences Center, New Orleans, LA.*

Purpose of Study: Describe the experience of a NCQA recognized tier 3 patient-centered medical home in New Orleans, LA that integrates mental health with primary care services.

Methods Used: We implemented a program for depression care using a Collaborative Care Model (CCM) involving co-located primary care providers (PCPs), care manager, social workers (SW), psychologist, and psychiatrist. All providers attend a workshop on the CCM. All patients get a 2 question screener at triage. If positive, they receive a Patient Health Questionnaire (PHQ9). Guidelines indicate monitoring with PHQ9, scores >10 prompt monthly follow up and repeat until <5. PCPs refer as needed for psychiatry consultation or counseling by SW or psychologist. We used the electronic medical record to compare the following outcomes for one year pre- and post-intervention start date (October 1, 2008): prevalence of depression diagnosis, depressed patients with PHQ9, patients with PHQ9

>10 with repeat PHQ9, first follow up interval after diagnosis, receipt of counseling, and psychiatric consultation.

Summary of Results: Depression diagnosis increased from 4.1% (n=199) to 6.9% (n=317). The percent of depressed patients with a PHQ9 increased 22.1% to 63.7%. Among post-intervention patients with PHQ9 >10, 42.5% had repeat PHQ9. The mean interval to first follow up appointment decreased 13.6 to 6.7 weeks. Depressed patients seen for counseling increased 10.6% to 24.3%. Of 65 patients referred to psychiatry 23 had depression, of which 9 were seen.

Conclusions: In the first year, this medical home's mental health program improved depression recognition, follow-up, symptom monitoring and mental healthcare delivery. Most psychiatry consultations were for problems other than depression, which may indicate PCP comfort. The number of referrals lost to follow up may indicate stigma, cultural factors, or problems in the referral process which warrants further investigation.

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RESIDENT RATINGS OF INPATIENT COMPLEXITY RELATED TO PATIENT SELF-RATINGS: A QUALITATIVE STUDY

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Purpose of Study: In recent years, complexity of patient care has increased 20 fold and ratio of caregivers to patients exceeded 16:1. The purpose of this study is to investigate the variables of complexity involved in patient care from the perspectives of both resident physicians and hospitalized patients.

Methods Used: During a summer period, research assistants observed teaching rounds of Internal Medicine teams at a university hospital. After rounds, residents were asked to rate each patient's administrative, medical, provider, and psychosocial complexity on a 10-point, Likert-type scale (1=not complex, 10=very complex). Additionally, consented patients were asked to rate their own medical complexity (same 10-point scale) and give feedback regarding their status and care received. Descriptive statistics and factor analysis were completed with SAS 9.1. Qualitative data were analyzed by grounded response theory.

Summary of Results: Fifty-four completed patient survey instruments were collected. Of these, 43 responded to the open-ended item, "Right now, I feel my health care..." and 41 had corresponding complexity ratings from the residents caring for them. Overall, patients perceived their illnesses as more medically complex than residents (6.60 vs. 4.97, p=.0007). Rotated factor analysis of the resident survey yielded a two factor structure: medical/provider complexity and psychosocial/administrative complexity (Eigenvalues 2.58 and .933, respectively). Similarly, patients responded to the item about their health care predominantly in one of two domains: by perception of illness severity (e.g. "good", "getting better", and "deteriorating") or sense of being attended to. (e.g. "being taken care of", "in good hands", "feel good to be at UK", and "getting adequate care").

Conclusions: In this sample, analysis of resident ratings of inpatient complexity was found to be a two factor structure. Interestingly, this construct seems to be supported by near categorical qualitative analysis of patient responses. These data might be of use to future research for patient complexity measurement scales.

Southern Society of General Internal Medicine Research Abstract Session B

10:30 AM

Friday, February 26, 2010

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SUCCESS OF PRIMARY CARE-BASED HEPATITIS C TREATMENT FOR URBAN, UNDERSERVED PATIENTS

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Purpose of Study: Effective therapy for hepatitis C (HCV) is available, however accessing subspecialist care for this treatment is challenging for some patients. The Liver Clinic at Grady Memorial Hospital was founded by general internists to improve access to HCV care for urban, underserved

patients. The clinic serves primarily black patients, a group that has a higher prevalence of HCV infection and low response rates to HCV treatment. The purpose of this study was to assess the success rates of therapy for chronic HCV in this real world clinic that serves patients with difficult-to-treat characteristics.

Methods Used: Charts of all 870 patients who presented to the Liver Clinic from May 2002 to December 2007 were abstracted for demographic data, HCV genotype, viral load, fibrosis score, and medical co-morbidities using a standardized data collection tool. One hundred thirteen patients initiated HCV treatment during the study period. Results of virologic response to treatment were collected for this group and analyzed using an intention to treat design. Statistical analysis was performed using SAS.

Summary of Results: Of the 113 treated patients, 68% were black and 26% were white. Most patients were uninsured (67%). The majority of patients were genotype 1 (86%), and the remaining patients were genotype 2 (11%) and genotype 3 (3%). The mean viral load was 2.7 million copies. Sixteen percent of the patients had cirrhosis. The overall sustained virologic response (SVR) rate was 30%. The table shows SVR rate by race and genotype.

Conclusions: The SVR rate among genotype 1 black patients in this urban, underinsured population in a public teaching hospital was similar to the SVR rate achieved in clinical trials (19% compared to 19 - 28%). Successful treatment of HCV can be accomplished by general internists in a resource-limited setting among patients with difficult-to-treat characteristics. The Grady Liver Clinic can serve as model for primary care-based treatment of urban, underserved patients with HCV.

SVR Rate by Race and Genotype

SVR (%)	Genotype 1 (n=97)	Genotype 2 (n=12)	Genotype 3 (n=3)	Overall (n=113)
Black (n=77)	19	67	N/A	21
White (n=29)	22	63	100	41
All Races (n=113)	23	67	100	30

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ARE PSYCHOSOCIALLY COMPLEX INPATIENTS LIKELY TO BE DISSATISFIED WITH CARE?

LE. Kokajko, BE. Gish, MJ. Lineberry, CH. Griffith, JF. Wilson, AR. Hoellein *University of Kentucky, Lexington, KY.*

Purpose of Study: Patient satisfaction is an increasingly important patient outcome measure. However, little is known about predictors of inpatient satisfaction. We hypothesize that more complex inpatients are less satisfied with their care.

Methods Used: During a summer period, medical student research assistants observed internal medicine teaching rounds at a university hospital and recorded teams' activities, census, and time devoted to each patient. Residents were then asked to rate each patient's administrative, medical, provider, and psychosocial complexity on a 10-point, Likert-type scale (1=not complex, 10=very complex). After rounds, an anonymous survey instrument was administered to consented patients assessing satisfaction on a 4-item, 5-point Likert-type scale. Descriptive statistics, Pearson and Spearman correlations, and multiple regressions were analyzed with SAS 9.1.

Summary of Results: Sixty-four teaching rounds with 11 attending physicians were observed. The average census was 10±3. Of 127 completed patient satisfaction surveys, total satisfaction was 4.38±0.72. Mean rating of psychosocial complexity was 5.38±2.8. In the regression analysis, higher psychosocial complexity was predictive of overall poorer patient satisfaction ($F=6.41$, $p=.013$) especially when combined with high census ($F=8.77$, $p=.004$). When census was high, patients with high psychosocial complexity had a 28% chance of rating satisfaction with their care as very low (<4) whereas the base rate for very poor patient satisfaction was 8%. Patient complexity and census were not associated with time spent at the bedside or total time spent on the patient's case ($p>.05$).

Conclusions: In this sample of inpatients, those with complex psychosocial situations are more likely to be dissatisfied with their medical care particularly when team census is high. Such patients might be more aware or less forgiving of perceived hurry or distractedness by members of the inpatient team, or perhaps these patients' own traits account for their low satisfaction with care. Further research could investigate specific behaviors of the inpatient team and attitudes of patients that lend to higher or lower satisfaction scores.

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EVERY MINUTE COUNTS: DIAGNOSIS AND TREATMENT OF NEUTROPENIC FEVER IN THE EMERGENCY ROOM

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Purpose of Study: Neutropenic fever is a medical emergency requiring initial intervention in the emergency room. The Infectious Disease Society of America has established guidelines for the treatment of neutropenic fever of unknown etiology in cancer patients. We examined if appropriate antibiotics were administered to cancer patients with neutropenic fever in the emergency room in a timely manner. We hypothesized that antibiotics in accordance with IDSA guidelines would be administered within one hour of diagnosis of neutropenic fever in greater than 95% of patients, and that the correct antibiotics would be chosen based upon the guidelines.

Methods Used: Twenty-five patients presenting to the emergency room with a diagnosis of cancer and neutropenic fever were randomly selected. The following data was collected: Time from diagnosis of neutropenic fever to administration of antibiotics, cell counts, type of antibiotics administered, age, and gender.

Summary of Results: Forty-four percent of patients received antibiotics within an hour of diagnosis. Forty-eight percent of patients received the proper antibiotic regardless of time of administration. Interestingly, among patients who received antibiotics within one hour, the correct antibiotic was given 63% of the time. When antibiotics were not administered in a timely manner, the correct antibiotic was given only 36% of the time.

Conclusions: There are several possible reasons why there is a delay in antibiotic administration. (1) Failure of the ER physician to recognize neutropenic fever. (2) Systems delay in getting the physician vital signs and lab data so that a correct diagnosis can be made. (3) Systems delay in submitting orders or pharmacy getting the correct antibiotics to the ER. Since the results of this study are significantly below expectations, the following interventions are being considered for implementation: Stocking first line antibiotics in the ER to avoid delays in administration, educating ER physicians and nursing staff on IDSA guidelines, automated flagging of charts to alert ER staff to a possible neutropenic fever, and implementing a neutropenic fever alert system which would mobilize internal medicine residents more familiar with neutropenic fever to advise in the care of the patient.

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RATES OF HEPATITIS A AND HEPATITIS B VACCINATION IN AN URBAN, PRIMARY CARE-BASED HEPATITIS C CLINIC

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Purpose of Study: Patients with hepatitis C who become infected with hepatitis A virus (HAV) or hepatitis B virus (HBV) are at risk of accelerated progression to cirrhosis and fulminant hepatic failure. Experts recommend HAV and HBV vaccination for susceptible hepatitis C patients, but rates of vaccination remain low. The Liver Clinic at Grady Memorial Hospital is a primary care-based clinic that serves an urban, indigent population and provides comprehensive care for patients with hepatitis C. Rates of HAV and HBV vaccination have not been studied in this setting.

Methods Used: A retrospective chart review was performed on 870 Liver Clinic patients. Data were abstracted on hepatitis A and B immunity status and completion of vaccination series for HAV and HBV. Separate analysis of vaccination rates was performed for patients who received treatment for hepatitis C.

Summary of Results: For the total cohort, immunity status to HAV and HBV was checked in 75% and 82% of patients, respectively. Sixty percent of patients were potentially susceptible to HAV (had negative HAV total antibody or were not tested), and 74% to HBV (had negative HBV surface antibody and core antibody or were not tested). The rate of documented, completed vaccination in all potentially susceptible patients was 41% for HAV and 44% for HBV. Considering only patients with known serology, 70% and 72% of susceptible patients completed vaccination for HAV and HBV, respectively. For the treated cohort, vaccination rates for potentially susceptible patients were 58% for HAV and 68% for HBV. Considering only patients with known serology, vaccination rates were 100% for HAV and HBV.

Conclusions: The rates of vaccination for HAV and HBV in patients with chronic hepatitis C in our clinic are higher than reported for primary care

practices and comparable to or higher than some specialty practices. Still, rates of serologic testing and vaccination rates in our total cohort are sub-optimal and may be due to patient, physician, and system factors. Solutions addressing these will be necessary to improve vaccination rates.

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TRAJECTORIES OF ILLICIT DRUG USE AND HEALTH OUTCOMES AMONG ADULTS FOLLOWED FOR 18 YEARS (THE CARDIA STUDY)

S. Kertesz^{1,2}, Y. Khodneva¹, M. Safford¹, J. Richman¹, M. Pletcher³ ¹U. Alabama, Birmingham, AL; ²VA Med Ctr, Birmingham, AL and ³U. California, San Francisco, CA.

Purpose of Study: Characterizing long-term health outcomes of drug use in general population samples is difficult because use often declines with age and long-term follow-up is rare. The Coronary Artery Risk Development in Young Adults study (CARDIA) allowed us to test if the longitudinal trajectory of nonmarijuana drug use was associated with worse health at 18-year follow-up in a 4-city sample.

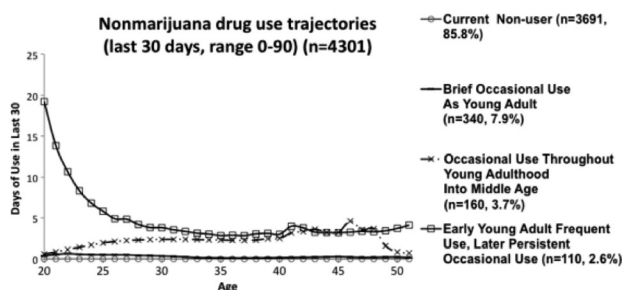


TABLE General Health Status at 18-Year Follow-up For 4 Drug Use Groups

	Current Nonusers (n=3691, 86%)	Brief Occasional Use as Young Adult (n=340, 8%)	Early Young Adult Frequent Use, Later Persistent Occasional Use (n=110, 2.6%)	Occasional Use Throughout Young Adulthood Into Middle Age (n=160, 3.7%)
Excellent/Very Good/Good	90%	86%	86%	77%
Fair	9.2%	13%	12%	18%
Poor	1.1%	1.2%	2.6%	4.4%

Chi-Squared (df=6) $p < 0.001$

Methods Used: Past month drug use was assessed at 3-5 year intervals in a biracial cohort of adults (n=4301) from 1987/88 (aged 20-32) to 2005/06 (aged 38-50). Subjects were sorted into groups based on their longitudinal drug use trajectory using semiparametric group-based statistical models. We compared drug trajectories for the outcome of general self-reported health (Excellent/Very Good/Good versus Fair and Poor). After converting health to a numerical value using the method of Diehr et al, we adjusted for demographics, alcohol, tobacco and baseline health.

Summary of Results: Four drug use trajectory groups were found (Figure). Drug use did not exceed 10 days per month in any group. At 18 years, persons with more persistent drug use were most likely to report Fair or Poor Health (Table), but adjusting for covariates rendered this difference nonsignificant.

Conclusions: Among young adults, more persistent nonmarijuana drug use was associated with worse general health status 18 years later. This observation was statistically explained by demographic characteristics and differences in baseline alcohol and tobacco use.

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PREPARING FOR ORAL PRESENTATIONS: VARIATIONS IN PREPARATION BY LEVEL OF TRAINING

ED. Snyder^{1,2}, A. Salanitro^{1,2}, A. Castiglioni^{1,2}, C. Estrada^{1,2} ¹UAB, Birmingham, AL and ²Birmingham VA Medical Center, Birmingham, AL.

Purpose of Study: Scientific presentation skills are expected in academic medicine and residency training. Development of these skills occurs with

time and experience. We sought to determine the differences in preparation for oral scientific presentations by training level.

Methods Used: Presenters at three academic general internal medicine (GIM) meetings received an e-mail invitation to complete an 11-item online survey. They were asked: 1) prior preparation frequency and settings; 2) type of feedback most helpful; and 3) changes made. Changes were grouped by content (focus, objectives, conclusions), visual aids (font, number of words, graphics, animation), and delivery style (mannerisms).

Summary of Results: Out of 279 possible, 182 presenters (62%) responded to the survey. 31% were trainees (medical students/residents), 12% fellows, and 56% faculty.

Practicing alone was the most common type of preparation, utilized by 79% of responders. Practicing in front of a group of more experienced colleagues was the most helpful type of preparation (38%), followed by practicing alone (26%), and sending slides to a mentor for review (13%). Data on training level are presented in the table.

Conclusions: Fellows were more likely to employ the most helpful ways to prepare for oral scientific presentations at academic GIM meetings. This may indicate increased access to a more formal mentoring system that is less available for trainees and faculty.

	All	Trainee	Fellow	Faculty	P Value
Practiced at least 4 times (%)	61	73	81	50	0.001
Practice Alone (%)	79	77	76	80	0.8
Slide review with mentor (%)	56	64	90	44	<0.001
Group of more experienced colleagues (%)	46	48	90	35	<0.001
Total changes made, mean (SD)	2.4 (1.7)	2.4 (1.5)	3.9 (1.8)	2.1 (1.6)	<0.001
Content Changes(%)	49	39	76	50	0.01
Visual Changes(%)	69	70	95	62	0.02
Delivery Changes(%)	26	46	33	13	<0.001

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MAINTENANCE OF CERTIFICATION: PARTICIPATION RATES AND PATIENT OUTCOMES

DM. Buscemi, H. Wang, MP. Phy, KM. Nugent *Texas Tech School of Medicine, Lubbock, TX.*

Purpose of Study: In 1990 the American Board of Internal Medicine started to issue time-limited certification. This decision represented the ABIM's goal to encourage internists to maintain up-to-date knowledge. The medical literature supporting this decision is limited, and this fact stimulated us to review participation rates and patient outcomes associated with this activity.

Methods Used: The medical literature was reviewed to identify outcomes studies which evaluated the effect of maintenance of certification (MOC) on patient care outcomes. The participation rates of internists with time-limited and life-time certification were determined.

Summary of Results: Several studies have shown a small positive association between patient outcomes and certification status. Holmboe measured the correlation between performance on MOC exam and designated QOC measures. Patients cared for by physicians in the top quartile on MOC were 17% more likely to receive all three diabetes processes of care indicators. Women were 14% more likely to have a mammogram. According to the ABIM, the participation rates in the MOC program among internists with time-limited certificates is 79%. Participation rates among internists with life-time certificates are unknown. A survey of the Internal Medicine leadership in various organizations reveals a low participation rate. The initial task force for the ABIM has a recertification rate of 18%. The ABIM board has a recertification rate of 20%. The editorial board for the Annals of Internal Medicine has recertification rate of 9%. The ACP Governors have a recertification rate of 6%. The ACP Board of Regents has a recertification rate of 27%. The ACGME-RRC Internal Medicine Committee has a recertification rate of 0%.

Conclusions: The ABIM decision to issue time-limited certification has a sound rationale. However, few clinical outcome studies have demonstrated any important patient outcomes related to this process. Participation rates by senior leadership in Internal Medicine have been unusually low. The ABIM needs to undertake additional studies to correlate patient outcomes with MOC status, and it should examine the relationship between other professional development activities and patient outcomes.

Southern Society of General Internal Medicine Research Abstract Session C

1:30 PM

Friday, February 26, 2010

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RESIDENT INPATIENT HANDOFFS: A MULTI-METHOD QUALITY IMPROVEMENT INITIATIVE

M. Burton^{1,2}, K. Charlton¹, C. Estrada^{1,2}, C. Ritchie^{1,2} ¹UAB, Birmingham, AL and ²Birmingham VA Medical Center, Birmingham, AL.

Purpose of Study: The handoff process is increasingly recognized as an important patient safety concern. We examined our current handoff process to guide the development of a computerized tool with the intent to standardize and improve handoffs.

Methods Used: We conducted a multi-method observational study of the handoff process between resident physicians on inpatient medicine units. Senior residents from each ward team scored their interns' handoffs for completeness and accuracy, and then identified medical errors related to the handoff. Interns were surveyed and directly observed to evaluate adherence to three key Joint Commission expectations: 1) The process includes interactive communication and opportunity for questions; 2) There is adequate opportunity to review relevant patient history; and 3) Interruptions are limited to not interfere with the handoff process.

Summary of Results: Among the 309 patients from 23 intern handoffs, demographic data, history, code status, allergies, and a to-do list were reliably present and accurate (>95%). Medications were present for 99% of patients, but 13% were inaccurate; likewise, recent events or anticipated changes were present 86% but 19% were not accurate. Only one error was identified.

We collected 26 intern surveys and observed 26 intern handoffs. Adherence to recommendations by survey and direct observation, respectively, were as follows: 97% and 92% for interactive communication, 93% and 92% for adequate opportunity to review relevant history, and 97% and 58% for limited interruptions. All handoffs were generated by word processing software, but no universal template was used.

Conclusions: Internal medicine residents reliably adhered to Joint Commission expectations, although their perceptions about interruptions underestimated direct observation. Almost all measured components of the handoff were complete and accurate with the important exception of 1 in 8 patients with an inaccurate medication list. This has important patient safety implications, and suggests the potential for health information technology solutions to make the process more robust and reliable, thereby reducing the potential for error.

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A QUALITY IMPROVEMENT INTERVENTION TO INCREASE HIV SCREENING IN PRIMARY CARE

B. Lea, K. Deep, J. Wilson *University of Kentucky, Lexington, KY*

Purpose of Study: Despite CDC recommendations that all patients ages 13 to 64 be screened for HIV, risk based testing continues to be the most common approach. Interventions that will lead to more widespread adoption of HIV screening are needed.

Methods Used: We developed an intervention based on a model of academic detailing to influence the HIV screening practices of a group of internal medicine physicians. The intervention group consisted of 6 attending physicians and 32 residents in a primary care practice at an academic medical center. The intervention consisted of: 1) face-to-face small group education sessions, 2) two large group didactic presentations, 3) electronic messages, 4) patient education handouts distributed by clinic staff, and 5) reminders in the exam rooms and clinical workspace. All 6 attendings and 11 residents participated in face-to-face academic detailing sessions. Rates of HIV were compared during a 60 day baseline period prior to the intervention and the 60 day study period. Descriptive statistical analysis and regression analysis were used to characterize the testing behaviors of the clinicians.

Summary of Results: In the baseline period, there were 1004 eligible patient visits and 19 HIV tests ordered for a screening rate of 1.9%. Ten males and 9 females were tested. During the intervention period, there were 912 eligible patient visits and 28 HIV tests ordered for a screening rate of 3.1% with 13 males and 15 females tested. The increase in HIV screening approached statistical significance ($p=0.99$). The mean age of patients receiving HIV tests increased from 35.4+11.1 years during baseline period to

44.3+11.6 years during the intervention period. Fifty-four percent of HIV tests ordered during the intervention period occurred during the first 20 days.

Conclusions: A multi-factorial academic detailing intervention resulted in an increase in HIV screening rates although the difference was not statistically significant. However, overall screening rates remained low. During the intervention period, physicians appeared to begin testing older patients. The effect of the intervention was more robust early in the intervention period and appeared to deteriorate over time. While this academic detailing intervention led to a change in physician behavior, a more systematic approach will likely be necessary to implement universal HIV screening.

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A CLUSTER-RANDOMIZED TRIAL OF A WEB-BASED PHYSICIAN INTERVENTION TO IMPROVE DIABETES CARE

C. Estrada^{1,2}, A. Salanitro^{1,2}, M. Safford², W. Curry^{1,2}, J. Williams², F. Ovalle², P. Payne-Foster³, Y. Kim², T. Houston⁴, J. Allison⁴ ¹Birmingham VA Medical Center, Birmingham, AL; ²University of Alabama at Birmingham, Birmingham, AL; ³University of Alabama at Tuscaloosa, Tuscaloosa, AL and ⁴University of Massachusetts, Boston, MA.

Purpose of Study: To assess a Web-based physician intervention on glycemic, blood pressure (BP), and lipid control in rural Southeastern US diabetes patients.

Methods Used: In 2006-7, 205 primary care physicians were randomized to control (a Web site providing links to diabetes-related information), or intervention (a multi-modal Web-based interactive intervention designed to improve diabetes care) groups. The intervention Web site included challenging cases, practical ideas to save time, guidelines, patient resources, and CME credit. Intervention physicians also received individualized Web-based performance feedback reports, using data they provided about their practice. All physicians provided 10-15 medical records of diabetes patients at baseline and follow-up over the 18 month intervention. Control-intervention group differences between baseline and follow-up proportions of patients with controlled A1c, BP, and LDL were assessed using generalized linear mixed models (GLMM).

Summary of Results: Of randomized physicians, 95 (46%) provided baseline (1,182 patients) and follow-up data (945 patients). Good control (% patients with A1c <7%, BP <130/80 mmHg, LDL <100 mg/dl, respectively) was similar at baseline and follow-up for the intervention (54.5% vs 55.5%; 41.9% vs 42.7%; 57.4% vs 56.8%) and control groups (55.3% vs 50.9%; 36.8% vs 39.6%; 55.0% vs 60.0%) ($p>0.05$ for all, including group*time interaction). Poor control (% patients with A1c >9%, BP >140/90, LDL >130) was similar or worsened between baseline and follow-up for the intervention (9.7% vs 11.7%; 8.1% vs 8.4%; 7.8% vs 11.3%*) and control groups (9.0% vs 15.0%*; 13.3% vs 10.1%; 9.0% vs 13.7%*) (* $p<0.04$, others $p>0.05$, respectively). Time effect and group-by-time interaction showed odds of poor control in A1c and LDL at baseline are less than odds of poor control at follow up (OR 0.67 (0.52 - 0.87) and 0.65 (0.49 - 0.85), respectively).

Conclusions: A Web-based multi-modal physician intervention was associated with less worsening of some diabetes performance measures over 18 months.

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ADDRESSING AND PREVENTING STRESS, FATIGUE AND BURNOUT IN HEALTH CARE PROVIDERS

M. Panda, C.J. Cunningham *University of Tennessee, College of Medicine, Chattanooga TN, TN*

Purpose of Study: Maintaining humanism is challenging for health care providers (HCP), especially when experiencing stress. ACGME recognizes negative effects of stress and recommends policies to prevent and counteract it. We instituted weekly Relaxing, Rejuvenating, Rejoicing in Residency sessions (RRRinRS) with the following objectives: (1) assess and monitor stress/fatigue/burnout among residents over 3 years, evaluate the effectiveness of RRRinRS intervention (2) Evaluate effectiveness of RRRinRS as means for recovery and fatigue/burnout prevention (3) Develop process for identifying residents at highest risk of burnout (4) Needs assessment for development of stress/recovery management training.

Methods Used: RRRinRS are held in hospital and are open to all HCP. Sessions provide encouraging environment to share information through

personal stories, book reviews, poetry, etc. Secure internet surveys were administered to medicine residents and core faculty and repeated quarterly to track responses. Surveys gathered qualitative data (general perceptions of personal stress/coping strategies) and quantitative data (stress, physical fatigue, burnout, life satisfaction, general health, coping styles, negative affectivity).

Summary of Results: Respondents (response rate=45%) indicating higher number of attendances reported significantly lower levels of exhaustion and pressure-related stress ($r=-.53/- .59$, respectively, both $p<.01$). Respondents with higher levels of negative affectivity reported higher frequencies of nonoptimal forms of coping (Avoidance and Emotional coping, $r=.48/.49$, respectively, $p<.01$) and indications of resource drain and strain. High negative affectivity was associated with higher levels of perceived stress. Qualitative evidence supported these coping behaviors, illustrating a need to teach residents more active problem focused coping techniques.

Conclusions: Preliminary results suggest that those who more frequently attended RRRinRS reported lower levels of stress than those who attended fewer sessions. Qualitative data provide insights into how HCP are recognizing and responding to stress. This data provides support for continued efforts to further refine and comprehensively evaluate the intervention as a strategy for improving stress and recovery management.

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CHARACTERIZING THE LONGITUDINAL PERFORMANCE OF INTERNAL MEDICINE RESIDENCY PROGRAMS WITH THE IN-TRAINING EXAMINATION

R. Nugent¹, D. Park¹, H. Wang², M. Phy², K. Nugent² ¹Carnegie Mellon University, Pittsburgh, PA and ²Texas Tech University, Lubbock, TX.

Purpose of Study: The internal medicine in-training examination provides residents and programs information about the residents' competence in medical knowledge and the programs' educational curricula. Currently the exam results are summarized with overall percent correct and residents' percentile standing. What is not generated is an overview of residents' performance over time, the programs' strengths and weaknesses, or comparisons between subgroups of residents.

Methods Used: We used all available 2000-2007 in-training examination results (100 residents; 209 exam records) for the Department of Internal Medicine at Texas Tech University in Lubbock, TX. For each resident, we calculate the percentage correct for each content area for each year the test was taken. We graphically summarize these longitudinal results to identify potential inconsistencies in both resident and program performance. We use ANOVA to compare the performance of incoming residents by calendar year and paired t-tests for residents' differences year to year.

Summary of Results: Selected results are presented in this abstract. The mean scores in the first year residents did not vary from year to year ($p>.05$) with the exception of Gastroenterology (low scores in 2001, 2005). Residents showed increases from the first year to the third year in all content areas ranging from 7.7% (General Internal Medicine) to 16.5% (Gastroenterology). All year to year differences were statistically significant (p -values<0.05) with the exception of Neurology and General Internal Medicine (both 2nd yr to 3rd yr). However, the patterns of improvement were dependent on the starting calendar year and medical education (US vs. nonUS).

Conclusions: By collecting more detailed statistics on residents' content area performance on the ITE, we can identify differences in how residents learn over time (possibly depending on their medical education and their starting calendar year). Trend lines do not indicate uniform improvement in all content areas; in particular, unexpected performance in some years (e.g. 2004) may indicate inconsistency in resident preparation, program curricula, or the ITE questions.

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USING STANDARDIZED PATIENTS TO TEACH ALCOHOL SCREENING

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Purpose of Study: To evaluate the effectiveness of using standardized patients with review of videotapes and feedback in improving residents' alcohol screening.

Methods Used: Twenty four postgraduate year one medicine residents completed 3 standardized patient (SP) stations regarding various communication

skills during their mandatory month-long Ambulatory Care Rotation from August 2008 through June 2009. From January 2009 to June 2009, an additional standardized station related to alcohol screening was introduced. The SP presented with insomnia and depression. Fourteen of these 24 residents completed the additional station. Each encounter was videotaped. The 14 residents reviewed their taped encounters with a faculty member and received faculty and SP feedback based on the National Institute on Alcohol Abuse and Alcoholism (NIAAA) guidelines. In September 2009 all 24 residents participated in an objective structured clinical examination (OSCE), which included a standardized case scenario in alcohol screening. The performance of residents in alcohol screening who previously received review of videotapes and feedback was compared with the performance of residents who did not receive review of videotapes and feedback. Faculty blinded to this designation observed the September 2009 OSCE station and completed a checklist based on the NIAAA guidelines. This study was approved by the IRB in the exempt category.

Summary of Results: Twenty four residents participated in the OSCE. Fourteen of these residents previously received review of videotapes and feedback regarding alcohol screening. Thirteen of these 14 residents asked any question related to alcohol use compared to 8 of 10 residents not receiving review of videotapes and feedback (93% versus 80%; $p>.05$). Residents who received review of videotapes and feedback were also more likely to ask an additional follow-up question related to assessing clinical impairment from alcohol use (50% versus 40%; $p>.05$). The results indicate a nonsignificant trend in this small sample size study.

Conclusions: In this pilot and feasibility study, a teaching intervention using SPs and review of videotapes and feedback may improve alcohol screening. We plan a larger study to better assess the effect of this type of educational intervention on alcohol screening.

Southern Society of General Internal Medicine Research Abstract Oral Plenary Session

9:45 AM

Saturday, February 27, 2010

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RECOGNITION AND MANAGEMENT OF CHRONIC KIDNEY DISEASE IN PRIMARY CARE

C. Litvin, P.J. Nietert, AM. Wessell, RG. Jenkins, SM. Ornstein *Medical University of South Carolina, Charleston, SC.*

Purpose of Study: Proper management of patients with chronic kidney disease (CKD) includes recognition of patients with the condition and interventions to prevent progression of renal disease and reduce risks for cardiovascular disease. Although the majority of these patients are treated exclusively by primary care providers, little is known about the quality of care they receive. The purpose of this study was to assess both recognition of CKD and adherence to treatment recommendations based on the Kidney Disease Outcomes Quality Initiative guidelines in a large nationwide representation of primary care practices.

Methods Used: This was a descriptive study performed in 120 practices participating in the Practice Partner Research Network, a network of primary care physicians using a common electronic medical record (EMR). All active patients over 18 years of age with a serum creatinine, age and gender documented in their EMR within a year as of March 31, 2009 were included in the analysis. Glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease equation. The proportion of patients with CKD, as defined as $GFR<60$, was calculated. Recognition was assessed by determining whether a diagnosis of CKD had been recorded in the EMR. Adherence measures for patients with CKD included prescription of an ACE-Inhibitor (ACEI) or Angiotensin Receptor Blocker (ARB), most recent blood pressure (BP) less than 130/80 mmHg, most recent LDL cholesterol (LDL-C) less than 100 mg/dl and avoidance of prescriptions for non-steroidal anti-inflammatory drugs (NSAID). All statistical analyses were performed using SAS v9.1.

Summary of Results: Among 237,920 patients meeting inclusion criteria, 14.6% had CKD. Of these, 93.8% had moderate disease (GFR 30-59), 4.9% had severe disease (GFR 15-30) and 1.3% had end-stage renal disease (GFR<15). Of all patients with CKD, 16.8% had a diagnosis of CKD recorded. 52.2% of patients with CKD had received a prescription for an ACEI or ARB, 39.7% were at the BP goal, 45.7% were at the LDL-C goal and 13.4% had been prescribed an NSAID.

Conclusions: CKD is common in primary care practices. Under-recognition may be responsible for suboptimal adherence to treatment guidelines. Interventions to improve the identification and management of patients with CKD could have a major public health impact.

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USE OF ECOLOGICAL MOMENTARY ASSESSMENT TO IMPROVE A RESIDENCY CURRICULUM

LL. Willett¹, T. Wall¹, C. Estrada¹, W. Curry¹, S. Cohen¹, A. Salanitro¹, J. Ngu¹, H. Coley¹, T. Houston² ¹University of Alabama at Birmingham, Birmingham, AL and ²University of Massachusetts, Worcester, MA.

Purpose of Study: Ecological Momentary Assessment (EMA) is a brief, unobtrusive evaluation method occurring immediately after an educational experience. We sought to determine whether EMA could guide curricular change in a residency program.

Methods Used: Clinician educators developed an 8-item EMA tool to assess ambulatory morning report (AMR). Three AMR sessions were held weekly, each with a different format: general didactic presentation, board review questions, case presentation. For two consecutive years, AMR resident participants completed the EMA tool after each session. In year 1, baseline data measured the educational value of the 3 formats. We found the board review questions had the lowest scores, and AMR was valued least by upper level residents. In year 2, we replaced only the board review questions with a didactic session targeted at upper level residents. The same tool assessed the impact of the change. We used factor analysis with varimax rotation to measure the tool performance.

Summary of Results: We collected 1,369 evaluation cards (2007 n=836; 2008 n=533). Factor analysis suggested the items did not load well onto a single factor and measured separate constructs. Evaluations improved from year 1 to year 2 only for the session changed. Residents favored the new curricular format with responding yes definitely to: I would recommend today's AMR to a colleague (80% to 88%; p=0.02), the content was in an area needing personal improvement (72% to 84%, p=0.002). Residents responded favorably that more sessions should be modeled like today's (p=0.03) and other sessions should be cut to have more structured like today's (p=0.005). When stratified by year of training, only upper level resident evaluations improved from Year 1 to Year 2.

Conclusions: A new EMA tool successfully guided curricular changes in a residency program. The tool identified the session needing improvement, the level of training affected, and successful curricular impact.

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WEIGHING THE INFLUENCES: ADVICE SEEKING DURING RESIDENCY TRAINING

K. McKinney^{1,2}, M. Lineberry¹, J. Conigliaro^{1,2} ¹University of Kentucky Medical Center, Lexington, KY and ²Lexington Veteran's Administration Medical Center, Lexington, KY.

Purpose of Study: Inability of residents to respond appropriately to clinical uncertainty has been correlated with poor patient outcomes and adverse events. Observational data and "ad hoc" opinions suggest that advice-seeking as a response to clinical uncertainty is central to residency culture, however, little is documented regarding this behavior. We examined how medical residents seek advice when faced with clinical uncertainty in the inpatient setting.

Methods Used: We conducted audio-taped, semi-structured focus group interviews with University of Kentucky internal medicine resident physicians to discuss facilitators and barriers to advice-seeking during residency. Transcribed interviews were analyzed using grounded theory methodology with text coded via the constant comparative method. Trustworthiness and reliability of findings were addressed using ATLAS.ti qualitative data management software and an iterative process of code development.

Summary of Results: Six focus groups were conducted with 28 residents. Analysis revealed that residents' advice-seeking is dependent upon situation specific balances of facilitators and barriers. Primary facilitators of advice-seeking included the patient's clinical condition, the physical presence of an advisor, and service specific and inter-professional team relationships. Workload concerns, awareness of resources, and lack of knowledgeable source of help represented major barriers. Junior and senior residents, as well

as interns, recounted difficulties in asking for and obtaining help throughout training.

Conclusions: Our findings suggest the need to re-examine the infrastructure of support and supervision for trainees in the inpatient academic setting. The influence of availability and the physical presence of an advisor highlights the vulnerability of clinical decision making during duty periods such as night float and weekends. Moreover, the correlation between team relationships and seeking advice indicates the importance of establishing interdisciplinary teams on ward rotations. These findings signal a need for residency programs to intentionally discuss advice-seeking both early and repeatedly during training to better equip residents to handle clinical uncertainty.

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FRAILITY IN PATIENTS WITH CHRONIC LUNG DISEASES UNDERGOING PULMONARY REHABILITATION

N. Mittal, R. Raj, K. Nugent, A. Reddy *Texas Tech University Health Science Center, Lubbock, TX.*

Purpose of Study:

1. To determine the prevalence of frailty in patients with chronic lung diseases
2. To determine if pulmonary rehabilitation results in change in frailty
3. To simplify the process of screening patients who need a more detailed frailty assessment

Methods Used: 51 subjects from pulmonary clinic underwent evaluation for frailty based on weight loss, self reported exhaustion, 15-foot walk time, grip strength and physical activity in addition to a 100-foot walk. 9 of these patients underwent pulmonary rehabilitation. Data were abstracted and analyzed.

Summary of Results: Study population was characterized by 61% females and 39% males with a mean age of 67 years (33-89), mean BMI of 30 (15-63). COPD was the most common diagnosis (57%). 22% of these patients were frail, 63% pre frail and 16% were not frail. Frail patients were more likely to have degenerative joint disease (chi square, p=0.023) and slower gait speeds (frail:41m/min, pre-frail:50m/min, not-frail:65m/min, ANOVA, p=0.01). Prevalence of frailty decreased in patients undergoing pulmonary rehabilitation and frail patients were likely to derive the most benefit in terms of improvement in frailty markers (% benefiting from rehab: 75%frail, 25%pre-frail, 0%not-frail, chi square, p=0.024). Gait speed increased in patients overall after pulmonary rehabilitation(pre:48.0m/min, post:54.9m/min). Patients with slowest initial gait speeds were more likely to show an improvement in their gait speed after rehabilitation(Pearson's coefficient=-0.602, p=0.011). Patients with initial gait speed slower than 60m/min on a 100-foot walk test have a 91% chance of being frail while the ones with gait speeds greater than 60m/min have 88% chance of not being frail.

Conclusions: (1)Frailty is common in patients with chronic lung disease.

(2)Frailty improves with pulmonary rehabilitation and frail (rather than pre frail or not frail) patients are likely to derive the most benefit from rehabilitation. (3)Gait speed cut-off of 60 m/min on a 100-foot walk test has a high sensitivity and specificity to identify patients with or without frailty. This can simplify frailty assessment by assigning pretest probabilities to patients who can undergo a more detailed frailty assessment. Prospective studies are needed to confirm these findings.

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NEUROCOGNITIVE DEFICITS IN ADULTS WITH SICKLE CELL DISEASE

N. Thrash, B. Goodman, I. Chen *Eastern Virginia Medical School, Norfolk, VA.*

Purpose of Study: Sickle cell disease (SCD) is often associated with multiple complications including increased risk of stroke and chronic pain that frequently requires opioid therapy. Studies have shown that patients with a history of stroke, chronic pain, and chronic opioid use often experience neurocognitive difficulties, but the incidence of impaired cognition in adults with SCD is unknown. We hypothesized that adults with sickle cell disease will have a relatively high prevalence of cognitive dysfunction.

Methods Used: A cross-sectional survey was performed on 50 adult patients with SCD presenting to the sickle cell clinic at EVMS. Patients were excluded if they could not give informed consent or were less than 18 years old. Demographic data including age, gender, and level of education were collected. Other data including last narcotic dose, average weekly narcotic

dose, breakthrough narcotic use, average and current pain, medication list, history of stroke, WBC, hemoglobin, reticulocyte count, LDH, history of pulmonary hypertension, pulmonary artery pressure, and oxygen saturation by pulse oximetry were obtained through chart review. We then performed two cognitive function tests on each subject to assess cognitive impairment: the mini mental state exam (MMSE) and the Freund clock drawing test. Scores of less than or equal to 24 on the MMSE and less than or equal to 4 on the clock drawing test represented cognitive impairment.

Summary of Results: Cognitive impairment occurred in 25% of patients affected by sickle cell disease. The Freund Clock Drawing Test was more sensitive in revealing cognitive impairment than the MMSE. Patients with a history of stroke were 3.7 times and patients with hypoxia were 5 times more likely to have cognitive impairment than those without. Recent dose of opioids was not related to cognitive impairment.

Conclusions: A significant (non-zero) proportion of adult sickle cell patients revealed some level of cognitive loss on the MMSE and the Freund Clock Drawing Test. The Freund Clock Drawing Test proved to be a better tool for detecting cognitive impairment than the MMSE. Further studies are needed to identify morbidity and mortality issues and possible interventions for patients with cognitive impairment.

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GASTRO-ESOPHAGEAL REFLUX SYMPTOMS RESPOND TO AN ORAL APPLIANCE USED FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA

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Purpose of Study: Existing evidence indicates Continuous Positive Airway Pressure (CPAP) reduces gastro-esophageal reflux disease (GERD) symptoms in patients with obstructive sleep apnea syndrome (OSAS). This study was designed to determine if another OSAS treatment modality, the oral appliance (OA), also improves GERD symptoms.

Methods Used: This prospective study of consecutive patients electing to use an OA for OSAS was performed at the EVMS/SNGH Sleep Disorders Center. Investigators utilized polysomnography (PSG) to establish the presence and severity of OSAS in adult (18–79 yr.) patients. OSAS patients electing OA therapy (N=56) visited 1 of 2 dentists skilled in OA use. No discussion regarding the potential utility of the OA in GERD occurred. Patients completed a validated GERD symptom questionnaire (Shaw, 2001) at the initial visit and after satisfactory use of OA. A score > than 15.5 (range 0–50) indicated GERD. The post questionnaire also queried subjective OA adherence. A group of bruxism patients utilizing bruxism appliances, serving as the control group, continues to be enrolled.

Summary of Results: A total of 56 patients with OSAS treated with the oral appliance completed the pre and post validated GERD questionnaire. (Male 32, Female 24, Mean age 54 ± 9 and BMI 31 ± 5.4), PSG data revealed an AHI 22 ± 19 and low SaO₂ 85 ± 5.6 .) Overall, there was a significant reduction in GERD symptoms. The overall pre-appliance GERD score revealed a mean of 5.8 and a post-appliance GERD score demonstrated a mean of 3.5, paired t-test, $p=.01$. There were eight patients manifesting pre-appliance GERD (score > 15.5) prior to the oral appliance and seven of these patients' symptoms improved. These patients had a pre-appliance GERD score mean of 20.5 and a post-appliance GERD score mean of 10.6, $p=0.04$. Five of the eight patients with pre-appliance GERD symptom scores of > 15.5 reduced their symptom scores to less than 15.5, which suggests not having GERD symptoms subsequent to oral appliance use.

Conclusions: The data suggest that the use of an oral appliance decreases GERD symptoms in patient with OSAS. This finding suggests that like CPAP, the OA improves GERD symptoms. The two dental practices continue to enroll the bruxism control group.

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SELECTING THE BEST CLINICAL VIGNETTES: SHOULD THE SCORING TOOL CRITERIA BE MODIFIED?

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Purpose of Study: To determine whether a clinical vignette scoring tool could be modified to improve its psychometric properties.

Methods Used: We compared the scoring tools for vignette submissions at a national general internal medicine meeting. At the 2006 meeting, the scoring tool comprised 3 criteria: clarity, significance, and relevance (with brief general descriptors). For the 2007 meeting extensive cognitive testing led to a revised tool with 5 criteria: clarity, significance, relevance, teaching value, and overall assessment (with more detailed descriptors). Both tools used a 7-point Likert scale. We calculated Cronbach's alpha (reliability) and performed factor analysis.

Summary of Results: We analyzed all 938 vignette submissions (2006, n=484; 2007, n=454). The 2006 scoring tool had a mean overall score of 4.98 (SD 0.67); the sub-scores were clarity 4.98 (SD 0.76), significance 4.98 (SD 0.70), and relevance 4.97 (SD 0.78). The Cronbach's alpha was 0.81; a one component domain accounted for 72.5% of the variance (Eigenvalue=2.18). The revised 2007 tool had a lower mean overall score of 4.68 (SD 0.68, $p<0.005$); the sub-scores were clarity 4.70 (SD 0.80), significance 4.76 (SD 0.71), relevance 4.68 (SD 0.68), teaching value 4.69 (SD 0.78), and overall assessment 4.60 (SD 0.77). The Cronbach's alpha was 0.95 for all 5 criteria, and 0.87 using the first 3 criteria (with expanded definitions); a one component domain accounted for 83% of the variance (Eigenvalue=4.15). On the revised 5-item tool, the inter-item correlation was highest for teaching value and overall assessment (0.90); all others ranged 0.65 to 0.88. If either teaching value or overall assessment were removed from the tool, the Cronbach's alpha decreased to 0.93 and 0.92, respectively. If clarity and relevance were deleted from the 5-item scoring tool, the Cronbach's alpha increased to 0.95.

Conclusions: The reliability of two scoring tools to select clinical vignette submissions is excellent and they measure a single domain. The addition of two criteria, teaching value and overall assessment, improved the psychometric properties of the selection process for clinical vignettes more than refinement of criterion descriptors alone.

Submitted but not Presented

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CORRELATION BETWEEN PLASMA AND URINARY ALDOSTERONE LEVELS IN PATIENTS WITH RESISTANT HYPERTENSION

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Purpose of Study: Measurement of 24-hour urinary aldosterone after oral sodium loading or while on a sodium replete diet is an accepted method to confirm the diagnosis of primary aldosteronism. This study aims to determine the correlation of plasma aldosterone values to urinary aldosterone levels in patients with resistant hypertension.

Methods Used: We evaluated 329 patients with resistant hypertension (51% males, mean age 54.9 years, 53% African American) who were referred to the hypertension clinic at the University of Alabama at Birmingham between 2004 and 2008, and underwent testing for plasma aldosterone, plasma renin activity (PRA) and 24 hour urinary aldosterone. Twenty four hour urine creatinine and sodium were used to assess adequacy of urine sample. The Pearson correlation coefficient and multiple regression analysis were used as statistical tests.

Summary of Results: The patients were taking an average of 4.08 antihypertensive medications. Mean body mass index was 32.6. Mean plasma aldosterone, PRA and 24 hour urine aldosterone levels were 12.41 ng/dL, 3.618 ng/ml/hr, and 12.05 mg/24 hours respectively. In univariate analysis, plasma aldosterone was correlated to 24 hour urine aldosterone ($r=0.545$, $p<0.0001$). In analyzing those patients with a high urine aldosterone level (>12 mg/24 hours) and patients with a low urine aldosterone, plasma aldosterone was correlated with both ($r=0.41$, $p=0.0046$ for high urine aldosterone, $r=0.38$, $p<0.0001$ for low urine aldosterone). In the multivariate linear regression analysis, plasma aldosterone is correlated to BMI and urine aldosterone levels but not to age and PRA values. A plasma aldosterone cut-off of ≥ 12 ng/dL has a sensitivity of 78%, specificity 62%, and a negative predictive value of 94% for predicting primary aldosteronism.

Conclusions: Plasma aldosterone is correlated to 24 hour urine aldosterone levels in patients with resistant hypertension.

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ASSOCIATION OF THE COOMBS' TEST WITH PNEUMOCOCCAL HEMOLYTIC UREMIC SYNDROME

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Case Report: We present a case of a toddler admitted for pneumonia with Streptococcal pneumoniae serotype 19A who later developed hemolytic uremic syndrome. Due to the anemia and thrombocytopenia, a Coombs' test was done. Positive results prompted a hematology evaluation. Based on this experience, we felt that many clinicians were unaware of the association between a positive Coombs' test and pneumococcal HUS. In this report, we present the utility of a positive Coombs' test as an adjunct to diagnosing pneumococcal HUS perhaps even before the renal insufficiency becomes evident.

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LOW INCIDENCE OF CORONARY DISEASE IN THE METABOLIC SYNDROME-VARIABILITY IN CULTURES

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Purpose of Study: Obesity linked to Diabetes Mellitus is the Epidemic of the 21st Century. The above diseases with lipid abnormalities, plus hypertension, are clustered under "metabolic syndrome"(MetS). This syndrome is related to coronary artery disease, whose incidence varies depending on the culture. Hispanics with MetS usually shows low coronary artery disease, when compared with the U.S.A.

Methods Used: We studied 169 patients (P) with MetS in Puerto Rico- a U.S. Hispanic Island. The purpose of the study is to study why Mets is less aggressive in Puerto Rico than in U.S.A. and its causes.

Summary of Results: 97% were diabetics Type II and 3% Type I. None showed myocardial infarction or stroke. The Ejection Fraction was reduced when compared to our normal group (49 ± 4 vs. $62 \pm 12\%$) $P < 0.001$ due to diabetic cardiomyopathy. The lipid profile was normal: HDL= 48 ± 16 , LDL= 83 ± 30 . Triglycerides 166 ± 13 , Cholesterol= 166 ± 25 [mg/dl]. 13% showed atrial fibrillation.

Conclusions: In U.S.A. a two fold increase in ischemic heart and strokes have been reported when compared to our data. We have shown that the expression of MetS accompanied with coronary artery disease is different in Puerto Rico than in U.S.A. Probably this is due to genetics and social networking, because Puerto Rico is the nation worldwide more influenced by U.S. culture.

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DIABETIC MYONECROSIS - AN UNUSUAL ENTITY LEADING TO ACUTE KIDNEY INJURY

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Case Report: Although a rare diagnosis, with very few reports in literature Diabetic myonecrosis is a complication of long standing uncontrolled diabetes mellitus should be considered as an etiology for Acute Kidney Injury. We hereby describe a 46 year old African American female with 9 year history of type 2 diabetes mellitus on Insulin with HbA1c of 10.4% presented to ED with painful left thigh swelling for 1 week with no traumatic injury. She was diagnosed to have of Inflamed lipoma and discharged home with analgesics. She revisited ED after 2 weeks with similar complaints. On examination, she was afebrile and had a diffuse, firm, tender swelling on the medial aspect of left thigh measuring 8*20cm with no fluctuance or erythema, her contralateral thigh being normal. Her muscle strength and motion were limited due to pain but sensation was intact. Pedal pulses were present bilaterally and ABI was normal. Lab tests revealed BUN and creatinine were elevated to 120 mg/dl and 5.2 mg/dl respectively from baseline 12 and 1.2. Serum Myoglobin was markedly high of 1695 ng/ml suggestive of Rhabdomyolysis. Urine analysis showed blood traces and no RBC. Renal Ultrasound and Doppler were unremarkable. Patient had Primary hyperparathyroidism with PTH of 135 pg/ml, calcium of 10.7mg/dl, albumin of 2.8g/dl and underwent parathyroidectomy. Doppler Ultrasound of lower extremities was negative for DVT. CT of left Lower extremity showed diffuse edema and enlargement of medial vastus with no localized fluid collection confirming the muscle infarction. Acute kidney injury was secondary to rhabdomyolysis which was secondary to muscle necrosis. After 5 days on supportive management which included IV fluids, analgesia and optimizing blood glucose control, acute kidney injury was resolved. Follow up after 6 weeks showed regression of swelling and at 10 weeks with complete resolution. Previous case series have shown Diabetes myonecrosis is seen in patients with poorly controlled and long standing diabetes, with recurrence upto 50%. In our case she returned with left lateral vastus muscle infarction after 2 months of prior episode. This case serves to

remind us that although diabetic myonecrosis is a rare entity causing acute kidney injury, should be kept in mind in a clinical setting of myonecrosis in a patient with uncontrolled diabetes mellitus.

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PULMONARY AND AXILLARY METASTASIS OF BASAL CELL CARCINOMA OF THE SKIN

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Case Report: 48 year old Caucasian male with a past medical history of skin cancer and healthy otherwise presented to our cancer center with a left axillary mass. Seven years earlier he was diagnosed with an ulcerated basal cell carcinoma (BCC) of the skin at his anterior chest wall that was resected multiple times. The size of the skin lesion was 4×6 cm at last resection and a skin graft was applied. The BCC recurred at the center the prior skin graft 4 weeks prior to developing the axillary mass. Aspiration of this mass showed metastatic poorly differentiated carcinoma with basilioid features. Staging was done by a positron emission tomography which showed multiple fluorodeoxyglucose (FDG) avid areas in bilateral lung fields and left axillary lymph nodes. He was started on a combination systemic chemotherapy with carboplatin and paclitaxel. He is awaiting evaluation for tumor response at the time of submission of the case report.

BCC is a common skin cancer in Caucasians. Although these cancers can be locally aggressive and destructive they have a very low predilection for distant metastasis. In one report, the rate of metastasis for a BCC was 0.1 percent. High risk feature have been identified by investigators which include but not limited to histological features, size, location, well versus poorly defined borders, number of recurrences, prior irradiation to the site.

Metastatic lesions usually occur in association with deeply invasive or large lesions.

Current chemotherapeutic agents are not very effective for metastatic disease. Metastatic BCC is typically fatal within one year.

Platinum containing agents have by far the most effective chemotherapy for this condition.

Most BCCs have abnormalities or mutations of Hedgehog pathway genes and this has prompted scientists to test inhibitors of this pathway for the control of local and metastatic cases. A recent phase 1 trial of an oral investigational drug has showed promise of antitumor activity.

We report an uncommon presentation of BCC of the skin with wide spread metastasis and review the literature regarding the known risk factors that may predict a more aggressive course and also explore the prior experiences with various chemotherapy regimens including the novel and investigational targeted therapy agents.

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A RARE PRESENTATION OF BILATERAL PHRENIC NERVE PARALYSIS IN A PATIENT WITH MULTIPLE MYELOMA

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Case Report: 47 year old healthy African American patient presented to the emergency room with shortness of breath and fever and was immediately intubated and admitted to the intensive care unit with respiratory distress. His physical exam was otherwise normal, had mild anemia, corrected calcium level of 15.1, total protein level of 11.9 gr/dL, creatinine of 3.3 g/dL and Quantitative IgG level was 8200 mg/dL. Serum and urine protein electrophoresis and immunofixation showed kappa light chain with a major restriction band in the gamma region. Bone survey showed diffuse lytic and osteoporotic bone disease and his plasma cells occupied more than 50% of his bone marrow cells. He was diagnosed with multiple myeloma (MM). His body fluid cultures including blood, HIV and hepatitis tests were all negative. Several days later his fever subsided and respiratory status improved. The next day after extubation he was found unresponsive with shallow breathing. Head CT scan was negative for an acute event. Blood gases showed respiratory acidosis due to hypoventilation with pH=7.19, pCO2=51 mm Hg and pO2=61 mm Hg. He was started on noninvasive bilevel positive airway pressure (BiPAP). In 24 hours of BiPAP usage his mental status normalized and thereafter he was BiPAP dependant. Patient had no signs or symptoms or laboratory evidence of myopathy. Chest X-ray compared to one done 4 months prior to the MM diagnosis and showed bilateral diaphragmatic elevation. His bedside negative inspiratory pressure test was low and with

fluoroscopy no diaphragmatic movement was detected with sniff test. Cervical spine compromise was ruled out by CT scan and he was diagnosed with MM associated peripheral neuropathy presenting as bilateral phrenic nerve paralysis. The patient refused diaphragmatic electromyographic and nerve conduction studies. He was started on high dose steroids for treatment of his MM and later was treated with cytoxan to avoid anti-myeloma agents that have neuropathies as side effects. His respiratory status gradually improved and was able to become BiPAP independent. Bilateral phrenic nerve paralysis is an extremely rare clinical presentation of the neuropathies that are associated with MM, the present case being the 3rd described in the literature, and which as in this case may be reversible with chemotherapy agents.

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IDENTIFYING POSTTRAUMATIC STRESS DISORDER IN A PEDIATRIC MOBILE CLINIC: TWO CASE STUDIES

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Case Report: The New Orleans Children's Health Project (NOCHP) is a pediatric mobile health program developed as a partnership between the Children's Health Fund and Tulane School of Medicine, Department of Pediatrics. NOCHP operates out of two state-of-the-art mobile clinics to provide a true medical home to its patients. One clinic offers free or low cost pediatric primary care services and the second mobile clinic provides mental health services to children and families. NOCHP services are provided in four underserved communities in the Greater New Orleans area.

The need for close collaboration between medical and mental health providers regarding the identification of posttraumatic stress disorder is illustrated in two case presentations of NOCHP patients. We discuss two patients, one of whom initially presented to the medical unit with a chief complaint of pruritic lesions and the other to the mental health unit for assistance for attention deficit hyperactivity disorder. Both patients presented with complaints unrelated to psychological trauma at their initial appointments but were later identified as having posttraumatic stress disorder related to their experiences with Hurricane Katrina. Both patients received services on both mobile units, thus providing them with an enhanced medical home. These cases illustrate the challenges experienced in identifying posttraumatic stress disorder (PTSD) in children in post-Katrina New Orleans. These challenges include the masking of PTSD symptoms by other behaviors such as hyperactivity or oppositionality, the tendency of providers to rule out PTSD in children who were not physically present in the hurricane, the general lack of knowledge and training in professionals regarding how to detect this disorder in children, as well as the problem of children having to be seen by adult providers due to the shortage of pediatric psychiatric providers.

In conclusion, these two cases illustrate the importance of the integration of mental health services into primary care, especially in a post-disaster setting. These cases also illustrate that our model of care on two mobile units is effective in providing high quality, comprehensive primary and mental health care to vulnerable patients without a medical home.

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STROKE DUE TO INADVERTANT PLACEMENT OF A HEMODIALYSIS CATHETER ACROSS THE ATRIAL SEPTUM

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Case Report: Hemodialysis catheters are widely used in hospital and outpatient settings. Although cardiovascular perforation is the most feared complication, other malpositions of a hemodialysis (HD) catheter can cause serious complications.

A 35-year-old woman with end-stage renal disease due to lupus had a split-type dual lumen tunneled catheter inserted through the right internal jugular vein for HD. During HD 13 months later she noted weakness of her left arm that progressed until she was unable to lift it. She had had a similar episode during her last HD that resolved spontaneously. Magnetic resonance imaging showed an acute right frontal lobe hyperintensity consistent with an ischemic stroke. A transesophageal echocardiogram (TEE) showed that the catheter entered the right atrium (RA) through the superior vena cava (SVC)

and crossed into the left atrium via a patent foramen ovale (PFO). Doppler exam and a bubble study showed no intracardiac shunt. A thrombus was attached to the right atrial side of the catheter at the area of the fossa ovalis.

Fluoroscopy showed that contrast injected through the arterial port entered the right atrium and flowed into the pulmonary artery; contrast put into the venous port entered the left atrium and flowed into the aorta. The catheter tip was withdrawn into the right atrium. She received anticoagulation for four weeks and showed rapid neurological improvement. Repeat TEE did not reveal any interatrial shunt.

Determining the best position for a catheter tip requires an understanding of numerous clinical variables including catheter type, insertion site, the patient's body habitus, and the intended use of the catheter. In general, the right atrial catheter tip is best placed at the junction of the SVC and RA. Catheters that are advanced farther have the potential for perforating the RA, entering the right ventricle and causing ventricular tachycardia, or crossing a PFO and becoming a source for systemic emboli. Because intravascular catheters can migrate, they should be firmly secured at the time of placement, and their position should be checked periodically.

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OBSERVATIONS ON THE THIRD COMMON NORMAL VARIANT OF ELECTROCARDIOGRAPHIC VENTRICULAR REPOLARIZATION

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Case Report: Three electrocardiographic (ECG) repolarization patterns are normal variants often confused with disease patterns. More has been written about early repolarization and persistent juvenile T-waves than about the 3rd pattern of lateral precordial ST-segment elevation with terminal T-wave inversion and a short QT interval.

We have studied 21 such patients. All were young (16-48 yrs old, mean 32) and black, and 19 were men. Six patients had only 1 ECG; 15 had 2-14 ECGs (mean 6) over periods of 2d to 10yrs (mean 25mo). The ECG pattern was stable in 7 of the 15, and it varied in 8, including changing back and forth to typical early repolarization in 3.

All ECGs showed J waves of different sizes, ST-segment elevations, and terminal T-wave inversions. Although these changes were often seen in the limb leads, they were maximal in leads V4, V5 except in 2 patients (1 woman) in whom the ST-T changes were more marked in the anterior and mid precordial leads.

The patients were seen for a variety of non-cardiac problems. Atypical chest pain was present in 6, but no cardiac cause could be found in any of them.

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UNEXPECTED SOURCE OF LOWER GASTROINTESTINAL BLEED

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Purpose of Study: Gastrointestinal (GI) bleed is responsible for 1-2% of hospital admissions in United States, therefore, lower GI bleed is common to see but lower GI bleed secondary to rupture of splenic artery aneurysm due to pancreatic necrosis is an uncommon cause of Lower GI bleed.

Methods Used: A 48-year-old male on coumadin for history of CVA in the past presented to emergency department from a nursing home for lower GI bleed. Along with this patient also complained of left-sided abdominal pain. Patient was a poor historian. Past medical history was significant for DM2, cognitive deficits secondary to brain injury, alcohol abuse, hypothyroidism, schizophrenia and history of pancreatitis as per chart.

On admission patient was awake, alert and responsive, his initial blood pressure was 70/47 mm Hg, pulse was 131 beats per minute, respirations were 20 per minute, oxygen saturation was 88% on room air and temperature was 98.4F. Abdominal examination showed hyperactive bowel sounds and generalized tenderness worse on left side. The rest of the examination was unremarkable.

Labs: Hb 7.2 g/dl, WBC 17.8, Plts 257, Na 143 K 4.6 Cl 114 BUN 18 Cr 1.2 Ca 7.7 HCO3 19 TP 5.1 Alb 2.2 TB 0.6 AST 21 ALT 16, amylase 20 Lipase 19, Lactate 2.6 and INR 2.26.

Summary of Results: CT scan of the abdomen showed splenic infarct, pancreatic calcification, a hematoma around the left colon and bleeding from splenic artery with possible fistula to colon. The patient underwent embolization of the splenic artery, however, he continued to have bleeding

so he underwent laparotomy which revealed peripancreatic necrosis eroding into a branch of the splenic artery and the splenic flexure of the colon.

Conclusions: A wide variety of diseases can present with lower GI bleed, keeping a broad differential diagnosis while approaching a lower GI bleed, helps in avoiding premature closure with the diagnosis.



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CONCURRENT MALIGNANCIES IN A CHILD WITH RELAPSED ACUTE LYMPHOCYTIC LEUKEMIA AND HODGKIN'S DISEASE AS A SECOND MALIGNANT NEOPLASM

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Case Report: Introduction: In children treated for acute lymphocytic leukemia (ALL), Hodgkin's disease (HD) as a second malignant neoplasm (SMN) is uncommon; more so two malignancies at the same time is a rare occurrence. The incidence of SMN after treatment for childhood ALL is reported to be 6-10 times higher than the general population. SMN is the second major cause of morbidity and mortality in this group following relapse of ALL.

Report: A 9 year old female with history of standard risk ALL, in complete remission (CR) & off treatment for 3 yrs presented for routine follow-up visit complaining of left neck swelling. On examination a 4 × 4.5 cm left lateral cervical lymphadenopathy (LDN) was noted & confirmed by CT scan. No other LDN was identified by physical exam or CT scan. Pathology report after lymph node (LN) biopsy revealed HD, nodular sclerosing type. While undergoing staging evaluation, her bone marrow examination surprisingly showed B-cell precursors ALL immunophenotypically similar to her original diagnosis. After confirmation of both malignancies at another large pediatric cancer center, the diagnoses of relapsed ALL & stage I A HD were made. The patient was reintroduced with vincristine, prednisone, doxorubicin, pegylated asparaginase & intrathecal methotrexate. She was in CR for both diseases at the completion of induction. Due to the coexistence of SMN and relapsed ALL she underwent peripheral blood stem cell transplant (PBSCT) from her HLA identical sibling with the conditioning regimen of total body irradiation, thiotepa and cyclophosphamide. She is currently 8 months post transplant off immunosuppression and remains in 2nd CR for ALL & 1st CR for HD.

Conclusion: With the dramatic improvement in the survivorship of children with cancer and specially childhood leukemia, the level of suspicion and surveillance for the development of SMN should be always present for these children. However, the concomitant development of these two malignancies has not been reported previously with a successful outcome after PBSCT.

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DIAGNOSIS BY RUPTURE: SPONTANEOUS HEMOPERITONEUM AS THE INITIAL PRESENTATION OF ADVANCED HEPATOCELLULAR CARCINOMA

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Purpose of Study: Spontaneous hemoperitoneum is an uncommon cause of acute abdominal pain. When it occurs, it may be catastrophic. Spontaneous rupture of hepatocellular carcinoma (HCC), a very rare cause of hemoperitoneum, is a life-threatening presentation, with an incidence of <3% of HCC patients in Western countries. The reported overall mortality is up to 50% in Asian countries, where the incidence is 12% to 14%. We present a case of spontaneous hemoperitoneum, in a patient without a previous diagnosis of HCC. We also review the incidence, etiological factors, diagnostic and management strategies for HCC.

Methods Used: The case report of a 47 year-old woman is described.

Summary of Results: A 47 year-old African-American woman, with a history of chronic Hepatitis C, presented with sudden onset of pain in the right upper quadrant of her abdomen. This was associated with near-syncope symptoms. Physical examination was significant for tense ascites and diffuse abdominal tenderness. Laboratory evaluation was significant for severe anemia with hemoglobin of 4.8 g/dL. A CT scan of the abdomen and pelvis revealed massive hemorrhagic ascites, associated with the rupture of a liver tumor, part of a multi-focal hepatocellular carcinoma. The patient was transfused packed red cells, and later underwent transcatheter arterial embolization (TAE) of her tumor.

Conclusions: Spontaneous rupture of HCC is a life-threatening condition; the mechanism is not clear but it is suggested that rupture is usually preceded by rapid expansion of the tumor secondary to intra-tumoral bleeding or venous occlusion secondary to invasion by the tumor. TAE is the immediate treatment of choice to obtain hemostasis. A second-stage hepatectomy may be undertaken if the lesion is resectable. Palliative therapy, including systemic chemotherapy with Sorafenib, may be the only option for advanced tumors; however, given the terminal stage of our patient's disease, she desired comfort care only.

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RELATIONSHIP BETWEEN BIRTHWEIGHT AND LONGITUDINAL CHANGES OF BLOOD PRESSURE IS MODULATED BY BETA-ADRENERGIC RECEPTOR GENES: THE BOGALUSA HEART STUDY

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Purpose of Study: Data on the genetic modulation of the effect of birthweight on blood pressure (BP), especially for longitudinal changes of BP, are scant. This study examines the genetic influence of β -adrenergic receptor (β -AR) gene polymorphisms (β 2-AR Arg16Gly and β 3-AR Trp64Arg) on the relationship of birthweight to longitudinal changes of BP from childhood to adulthood.

Methods Used: The study cohort consisted of 224 black and 515 white adults, aged 21-47 years, enrolled in the Bogalusa Heart Study. Data on birthweight and gestational age were obtained from Louisiana State birth certificates.

Summary of Results: Blacks showed significantly lower birthweight and frequencies of β 2-AR Gly16 and β 3-AR Trp64 alleles and higher BP levels and age-related trends than whites. In multivariable regression analyses, low birthweight was associated with greater increase in age-related trend of systolic BP (regression coefficient $\beta = -1.33$, $p < 0.0001$) and in diastolic BP ($\beta = -0.65$, $p = 0.006$) in the combined sample of blacks and whites, adjusting for the first BP measurement in childhood, race, sex, age, body mass index

and gestational age. β 2-AR Arg16Gly and β 3-AR Trp64Arg polymorphisms were not associated with BP age-related trend. Importantly, the strength of the association between birthweight and the increasing trend of BP, measured as regression coefficients, was modulated by the combination β 2-AR and β 3-AR genotypes for systolic BP trend ($p=0.024$ for interaction) and diastolic BP trend ($p=0.017$ for interaction), with blacks and whites showing a similar but nonsignificant trend.

Conclusions: These findings indicate that β -AR genes play a role in the genetic modulation of the intrauterine programming of BP regulation later in life.

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BLOOD PRESSURE VARIABILITY DURING CHILDHOOD IS ASSOCIATED WITH ADULT HYPERTENSION IN BLACKS AND WHITES: THE BOGALUSA HEART STUDY

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Purpose of Study: Blood pressure (BP) phenotype has two aspects, the level at a time point and the variability over time. This study tested the hypothesis that childhood BP variability, compared to levels, is more strongly associated with hypertension in adulthood.

Methods Used: The longitudinal study cohort consisted of 1797 adults (1091 whites and 706 blacks; 44.4% males; age=21-48 years.). Subjects were examined serially 4-8 times for BP during childhood (age range=4-19 years), with 9035 measurements of BP. Quadratic curves of childhood BP versus age were constructed. The childhood BP variability was measured as rate of change (variability I), residuals from age-predicted values (variability II) and residuals from the overall mean values (variability III).

Summary of Results: The overall prevalence of hypertension in adulthood was 14.1% ($n=253$), with blacks having a higher prevalence than whites (19.6% vs 10.5%, $p<0.001$). Blacks also showed significantly greater childhood BP variability I and III than whites for systolic BP. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by multivariate logistic regression analyses, using adulthood hypertension status as a dependent variable, adjusting for covariates. As shown in the table below, hypertension in adulthood was significantly associated with measures of BP variability during childhood except for systolic BP variability II. Further, the childhood BP variability was a stronger predictor of adulthood hypertension than childhood BP levels, although the levels were also significantly associated with adulthood hypertension.

Conclusions: These findings by showing a stronger association between childhood BP variability and adulthood hypertension suggest that the response of BP to environmental factors during growth and development may play an important role in the development of hypertension.

Odds ratio (OR) of childhood BP variability measures for adulthood hypertension, adjusting for race, sex, adulthood age and BMI, childhood mean BP levels and BMI variability (* $p<0.001$)

	Systolic BP			Diastolic BP		
	Variability I	Variability II	Variability III	Variability I	Variability II	Variability III
OR	1.16*	1.09	1.12*	1.18*	1.20	1.19*
95%CI	1.10-1.24	0.99-1.20	1.06-1.19	1.08-1.30	1.10-1.31	1.11-1.28

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BRAIN AND SPINAL CORD METASTATIC LESIONS FROM ESOPHAGEAL CARCINOMA: DIFFERENCES FROM SQUAMOUS CELL VS. ADENOCARCINOMA. PRESENTATION OF A CASE AND LITERATURE REVIEW

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Case Report: There are two types of esophageal carcinoma, squamous cell carcinoma and adenocarcinoma. Unfortunately, few patients survive beyond one year with either types of carcinoma. Spinal cord metastasis from primary esophageal cancer is extremely rare and has been reported in the literature in only two prior studies. Additionally, the presence of intramedullary metastatic lesions is more infrequent.

In this study, we report a patient with esophageal adenocarcinoma metastases to both the brain and spinal cord. We also reviewed the literature further to establish radiological differences and prognosis between esophageal adenocarcinoma and squamous cell carcinoma.

Compared to adenocarcinoma, intracranial metastases from squamous cell carcinoma of the esophagus are more likely to present with cystic lesion or peri-tumoral edema on CT and MRI images. However, higher incidence of spinal metastases and primary intracranial metastases occur more frequently with adenocarcinoma. An extensive workup including brain and spine MRI should be especially considered when early CNS manifestations are noticed in order to target an aggressive multi-modality therapeutic plan.

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UNILATERAL LHERMITT'S SIGN IN 57 YEAR-OLD MAN AFTER RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF NECK

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Case Report: Case report: A 57 year-old fair-skin Caucasian-American man developed unilateral shock-like sensations which radiated down to his spine and left lower extremity after radiotherapy for recurrent squamous cell carcinoma of the neck. The patient had a life-long history of sun-exposure. Two years earlier, he noticed 0.7 mm skin lesion on the left cheek. Wide local excision with advanced facial flap was carried out and pathologic report showed well-differentiated squamous cell carcinoma with perineural invasion and negative margins. For the next 13 months, the patient did well without recurrent lesions or symptoms. However, the patient subsequently developed 1.3 mm cord-like lesion at the left mandibular angle. The lesion progressively lengthened and surgical biopsy showed recurrent squamous cell carcinoma with perineural invasion. The patient was managed by salvage intensity modulation radiotherapy (IMRT) over the next 39 days. Five months after patient completed radiotherapy, he developed shock-like sensations which radiated from the neck to the left back and down to left lower extremity and were associated with neck flexion.

Discussion: Lhermitte's sign was typically described as shock-like sensation which traveled down the spine and to the lower extremities associated with flexion of the neck. Lhermitte's sign occurs secondary to injuries to oligodendrocytes which result in gradual demyelination of ascending sensory fibers. Besides radiotherapy, Lhermitte's sign is also associated with cobalamin deficiency, trauma, subacute combined degeneration of the spinal cord, cisplatin therapy, herpes zoster, bone marrow transplantation, cystinuria, Behcet disease, and multiple sclerosis. Lhermitte's sign is a common complication of radiotherapy which involves the spinal cord. The latency period ranges from 1-29 months after the end of radiotherapy. In most cases, spontaneous recovery occurs after 5.3 months although permanent damage may also occur. The chance a person may develop Lhermitte's sign increases with total radiation dose greater than 50 Gy, dose per fraction greater than 2 Gy, and with ages younger than 65.

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A REVIEW OF PLATELET TRANSFUSION PRACTICES IN THROMBOCYTOPENIC NEWBORNS

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Purpose of Study: Although thrombocytopenia is an uncommon occurrence in healthy term newborns, it is considerably more common in preterm and sick term newborns. It has been estimated that 2-9.4% of neonatal intensive care unit (NICU) admissions will receive platelet transfusions. A transfusion of 10 ml/kg is expected to increase platelet count by 50k/mm³. There are several unresolved issues regarding platelet administration, including the volume to administer and the duration of the transfusion. This study will investigate any effect of duration or volume of platelet transfusions on the resultant post-transfusion platelet count.

Methods Used: This is a retrospective study of the platelet transfusions administered to term and preterm infants admitted to the Children's Hospital of Oklahoma NICU in 2007 and 2008. The volume and duration of the transfusions were ordered at the preference of the attending

neonatologist; the effects on post-transfusion platelet counts were analyzed via parametric, non-parametric, and multivariate logistic regression models.

Summary of Results: Adequate documentation existed for 449 of the 520 recorded transfusions. None of the analyses of the data reached statistical significance. However, when transfusions of <1h were compared with those of ≥2h, the shorter transfusion times tended to have a greater increase in platelet number (72.5k/mm³, [-9, 169] vs. 50k/mm³, [-54,310]; p=0.3) despite having a smaller volume of platelets transfused (16cc/kg, [8,22] vs. 19cc/kg, [8,36]; p=0.2). With these parameters, a trend was also detected (using multivariate logistic regression analysis after adjusting for volume) that favored an increase in platelet count for babies with shorter transfusion times (p=0.1). In addition, there was a trend toward having > 50k/mm³ increases in post-transfusion platelet counts in a greater percentage of babies who received transfusions over <1h compared to ≥2h (43.7% vs. 26.4%, p=0.12).

Conclusions: Though the data did not reach statistical significance, there were trends that seem to favor shorter transfusion times, such as a greater increase in platelet counts with less volume. Future randomized controlled trials of different transfusion times with standardized volumes would be useful.

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SYPHILIS: THE GIFT THAT KEEPS ON GIVING

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Case Report: Primary adrenal insufficiency can be caused by multiple etiologies. We present a case that demonstrates an association between untreated neurosyphilis and primary adrenal insufficiency.

A 52 year old man with hypertension and migraine headaches presented with left sided weakness after a syncopal episode associated with a "different" headache and blurry vision for the past few weeks. There was no witnessed seizure activity and the patient denied additional prodromal warning signs or symptoms. Pertinent physical exam findings on admission included profound orthostatic hypotension, left upper and lower extremity weakness 4/5, and left visual acuity 20/40 with optic neuritis diagnosed by fundoscopic examination. The MRI and MRA of the brain were normal as were the carotid ultrasound, complete metabolic panel, and thyroid studies. Pertinent labs included an HIV which was nonreactive, positive hepatitis C antibody, RPR titer 1:1 and reactive TPHA. A lumbar puncture revealed a CSF white blood cell (WBC) count of 2/mm³ with 100% lymphocytes, increased protein of 67 mg/dL, normal CSF glucose, and negative CSF VDRL. With the "new" headache, elevated CSF protein, and optic neuritis, the patient was diagnosed with symptomatic neurosyphilis and treated with high-dose IV aqueous penicillin G for 14 days. Since he remained orthostatic despite fluid resuscitation, a 6 am cortisol level was drawn which was very low at 2.2 mcg/dL with a normal aldosterone level. A cosyntropin stimulation test confirmed the diagnosis of primary adrenal insufficiency. Physiologic doses of hydrocortisone were initiated with concurrent saline infusions until complete resolution of the orthostasis. The patient's blurry vision, orthostasis, left-sided weakness, and headache finally resolved with both penicillin therapy and steroid replacement.

Although the most common cause of primary adrenal insufficiency is autoimmune adrenalitis; infections, malignancy, hemorrhage, infarction, and drugs are also notable causes. This case highlights the importance of considering primary adrenal insufficiency in patients diagnosed with neurosyphilis.

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AN INCIDENTALOMA OF EXTRAMEDULLARY HEMATOPOIESIS

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Case Report: Extramedullary hematopoiesis is most likely to occur during fetal life; however, it can occur as a compensatory mechanism in different types of anemia.

A 56 year-old woman with a history of depression presented with a one week history of abdominal pain described as diffuse, sharp, intermittent, and a 3/10 on the pain scale. It lasted 5-10 minutes during attacks with no

radiation and was slightly worse with meals. She had one episode of nonbilious, nonbloody vomiting the day of presentation, decreased appetite secondary to pain, and a five pound weight loss over 4 months. She denied any changes in bowel movements, melena, or hematochezia. Mild tenderness to percussion of the epigastric area was present on exam. The vaginal and rectal exams were normal including stool being hemeoccult negative. Laboratory values were significant for hemoglobin 5.6 g/dl, hematocrit 19.1%, platelets 128,000/μl, MCV 50.5 FL, and RDW 32%. The differential was significant for 1% nucleated red blood cells and 1% immature mononuclear cells. Peripheral smear was consistent with anisocytosis, microcytes, target cells, tear drop cells, and dimorphic RBCs. An iron profile revealed iron 5 μg/dl and percent saturation 1%. EGD and colonoscopy revealed a nonbleeding, deep-cratered ulcer on the angularis of the stomach, chronic gastritis, and three sessile colon polyps (3-7mm in size). Biopsy of the stomach was consistent with chronic active gastritis with H. pylori organisms. Biopsies of the polyps revealed tubular adenomas. CTA of the abdomen and pelvis revealed two low density structures within the bilateral liver lobes, mild splenomegaly and a heterogeneous mass in the pre-sacral region. CT guided biopsies the liver hypodensities showed normal bone marrow elements including maturing myeloid and erythroid components and megakaryocytes, consistent with extramedullary hematopoiesis. CT guided biopsy of the sacral mass was also consistent with extramedullary hematopoiesis.

Extramedullary hematopoiesis presenting in multiple organs including pre-sacral masses have been reported in patients with hemoglobinopathies, most frequently, thalassemia. Further workup including electrophoresis and bone marrow biopsy may be required to determine if this patient has an underlying hematologic disorder.

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MYXOMATOUS MIX UP

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Case Report: Myxomas are rare, usually benign, intracardiac tumors composed of mucopolysaccharides. Almost all myxomas are found attached to the endocardium in the atria with vast majority being on the left side.

A 59 year old male with a history of tobacco and intravenous drug abuse presented with complaints of chest pain for one day. The pain was described as substernal, nonradiating, intermittent, self limiting, nonpleuritic and was not associated with shortness of breath, nausea, vomiting, or diaphoresis. He recently took flight from New York to New Orleans 5 days prior to admit and stated his last IV drug use was "several months ago." On presentation, he had a low grade temperature of 99.1oF. Physical exam was pertinent for a 2/6 holosystolic murmur and multiple homemade tattoos. Admit labs revealed a troponin of 0.16, and a new diagnosis of hepatitis C and HIV. EKG had no significant abnormalities. The patient refused an angiogram; therefore, a CT angiogram was ordered but could not be completed secondary to extravasation of contrast out of the IV site. A CT with PE protocol was negative. Transthoracic echo was consistent with severe mitral regurgitation with a vegetation attached to both mitral leaflets. Blood cultures were sent and vancomycin and gentamycin were started suspecting infectious endocarditis. TEE was subsequently done, and it was determined that the severe mitral regurgitation was due to a myxoma on the mitral valve with partial cordial rupture. Based on the large atrial size it was also believe to be a chronic process.

His presentation may have been secondary to the myxoma; however he refused further testing for an acute coronary syndrome and further inpatient evaluation of the myxoma. He requested follow up at his primary care physician's office in New York and will undergo a surgery evaluation for possible removal of the myxoma. Treatment for myxomas involves surgical removal with continued surveillance to assure that they do not recur.

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ORGANIZING PNEUMONIA IN MYELODYSPLASTIC SYNDROME: A RARE ASSOCIATION

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Case Report: A 56yo man presented with 2 months of cough, shortness of breath, anorexia and weight loss. He denied fever, night sweats or other

symptoms. PMH: negative, smoked for 20y, rare beer. PE: cachectic man with basilar crackles and heme neg stool. Lab: Hgb 5.1, MCV of 103, smear with schistocytes and target cells. CT: bilateral infiltrates and effusions. BM biopsy: myelodysplastic syndrome (MDS), ringed sideroblasts type. The patient required intubation 2 days later despite antibiotics. Thoracentesis showed an exudate but otherwise negative. Sputum and pleural fluid cultures, AFB and fungal cultures, urine streptococcal and Legionella antigens were negative. Extensive testing for connective tissue and autoimmune disorders was neg. B12 and folate: normal; ESR: 119 c/w the underlying MDS. The pt failed to improve with antibiotics so they were stopped. Bronchoscopy with bronchoalveolar lavage (BAL) revealed pulmonary macrophages and inflammation with negative bronchial fluid studies. Suspecting organizing pneumonia, the pt was started on steroids with improvement in his clinical and pulmonary findings.

Discussion: A variety of different pulmonary findings have been associated with MDS, including infectious and interstitial pneumonias, lymphoma, amyloidosis, bronchiolitis obliterans with organizing pneumonia (BOOP) and sweet syndrome. BOOP and organizing pneumonia are now used interchangeably to indicate a specific pattern of lung findings. Organizing pneumonia is associated with excess granulation tissue and inflammation in the bronchioles. On CT one sees patchy consolidation predominantly in the periphery and lower lung zones and bronchial wall thickening. PFTs usually show mild to moderate restrictive defects. BAL typically shows decreased macrophages and increased neutrophils, lymphocytes and eosinophils. While our case illustrates organizing pneumonia associated with MDS, it has also been linked to infections, drug injury (5-ASA, bleomycin, and amiodarone among others), collagen vascular diseases and radiation therapy. Steroids are often helpful but with frequent relapses. Cyclophosphamide and azathioprine have been effective though they remain unproven. Our case reminds physicians to think of organizing pneumonia when patients do not respond clinically to appropriate antibiotic therapy.

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HYPERKALEMIA FROM TRIMETHOPRIM SULFAMETHOXAZOLE THERAPY

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Case Report: Trimethoprim sulfamethoxazole (TMP-SMX) is a common cause of hyperkalemia that is commonly overlooked in the non-HIV population. This report will discuss and review hyperkalemia caused by TMP-SMX.

A 63 year-old man with a history of systolic heart failure, chronic obstructive pulmonary disease, type 2 diabetes, hypertension, peripheral vascular disease, prostate cancer, and stage 3 chronic kidney disease presented to the emergency department at the request of his primary doctor because of an abnormal serum potassium level of 6.1 mmol/L. The patient was undergoing pre-operative evaluation for resection of his prostate cancer the following week and was receiving TMP-SMX empirically. At admit, vitals included blood pressure 92/50, respiratory rate 12, temperature 98.2 °F, and pulse 87. Respiratory, cardiovascular, abdominal and neurologic examinations were unremarkable. Initial serum chemistries collected in the emergency room revealed a potassium concentration 5.5 mmol/L, BUN 40 mg/dl, and creatinine 2.7mg/dl. ECG showed normal sinus rhythm with non-specific ST-T wave changes. The patient's TMP-SMX was stopped and he was treated with kayexalate and calcium gluconate. On withdrawal of his TMP-SMX his potassium normalized to 5.3 mmol/L on discharge.

Adverse effects of TMP-SMX in the immunocompetent population are seen in 6-8% of patients. Many times the only side effects reported or noted are the common side effects (i.e. GI intolerance and skin rashes). Hyperkalemia is often not attributed to TMP-SMX use in these patients. Hyperkalemia, associated with the use of TMP-SMX, occurs secondary to its action on the collecting tubule where TMP-SMX mimics the activity of potassium-sparing diuretics and blocks the sodium channels. This effect is exaggerated with patients who have underlying kidney disease or if patients are on a second agent with potassium sparing effects (such as angiotensin-converting enzyme inhibitors and potassium-sparing diuretics). This case report emphasizes the need to increase awareness of hyperkalemia secondary to low dose TMP-SMX use in patients on ACE inhibitors and chronic kidney disease in the non-HIV+ population.

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CROHN'S DISEASE CAUSING VULVOVAGINITIS IN AN 8 YEAR OLD

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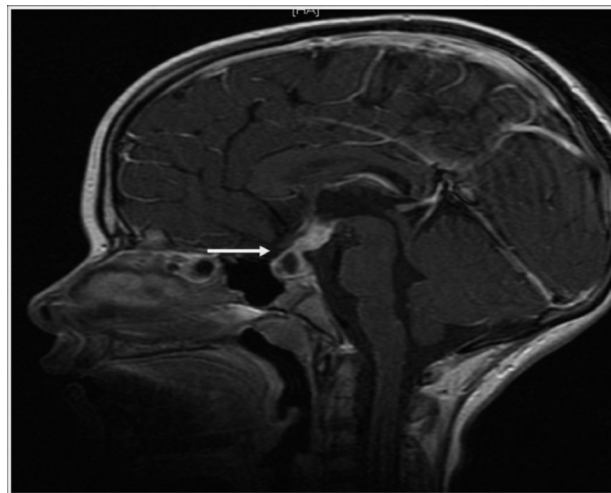
Case Report: Crohn's disease (CD) is a chronic, relapsing inflammatory disease that can affect the whole length of the gastrointestinal tract. Extra-intestinal manifestation commonly involve the joints, eyes and the skin. Vulvovaginal involvement although sporadically encountered in adult population is extremely rare in the pediatric patients with inflammatory bowel disease. We present a case of an 8 year old African American girl, previously diagnosed with CD 8 months ago presented with significant vulvar swelling, erythema and pain. Initial evaluation revealed an exacerbation of her CD. An infectious or a gynecologic pathology was ruled out with appropriate testing. A vaginostomy and proctoscopy in addition to radiologic testing failed to reveal any fistulas. A presumptive diagnosis of vulvovaginitis secondary to metastatic CD was made and a decision to initiate Infliximab was made. Patient's symptoms post Infliximab infusion improved significantly providing complete relief of vulvovaginitis. Vulvovaginitis poses a distinctive problem in the pediatric population secondary to initial impressions that can include possible sexual abuse, local infection, or a foreign body, however, although rare, it could possibly be the initial presentation of patient's CD. Furthermore in a patient with known CD, any vulvovaginal involvement should be considered as metastatic CD. A review of similar cases with regards to management of patients with metastatic CD involving the vulvovagina have revealed ineffectiveness of steroids and immune-modulator drugs. Scheduled Infliximab infusions have shown promising results in controlling the vulvovaginitis as it did in our patient.

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LYMPHOCYTIC HYPOPHYSITIS AND AUTOIMMUNE THYROIDITIS: A CASE REPORT

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Case Report: A 10 year old Caucasian girl presented with intermittent vomiting of 10 month duration and headaches for past 6 weeks. Initial evaluation including metabolic profile and blood cell counts were within normal limits. Patient had a normal upper GI endoscopy, but was found to have autoimmune thyroiditis. In view of unremarkable physical examination, lab data and normal MRI of the brain she was diagnosed with cyclic vomiting syndrome. Patient's symptoms continued to worsen and a repeat MRI of the brain showed a suprasellar mass with enhancement of the pituitary stalk. The radiologic characteristics suggested differential diagnosis including Pilocytic



Astrocytoma, Histiocytosis X, Hamartoma of the tuber cinereum, Sarcoid and lymphocytic hypophysitis (LYH). Serum and cerebrospinal fluid evaluations failed to reveal specific etiology of the pituitary lesion. Surgical intervention to obtain biopsy of the mass using a transphenoid approach resulted in drainage of purulent fluid from the sella upon incision of the dura. No organisms were identified and tissue histology showed numerous inflammatory cells within the pituitary which was consistent with the diagnosis of LYH. Patient's serum tested positive for *Macaca mulatta* antipituitary antibodies. Post surgery patient's symptoms resolved, she continues to have central diabetes insipidus and growth hormone deficiency as part of lymphocytic hypophysitis.

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IATROGENIC HYPERGLYCEMIC-HYPERINSULINEMIC STATE IN A PATIENT WITH NEPHROGENIC DIABETES INSIPIDUS

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Case Report: Introduction: Severe polyuria and hyperglycemia refractory to high dose insulin therapy developed in the post operative period following a colon resection in a patient with chronic lithium induced nephrogenic diabetes insipidus. Prolonged post-operative ileus required treatment with parenteral water replacement and total parenteral nutrition (TPN).

Case Report: 53 yr old male with rectal cancer developed progressive hyponatremia in the post-operative period after a partial colectomy. Pre-operative creatinine and post prandial glucose concentrations were 2.5 mg/dl and 141 mg/dl, respectively. His family reported that he chronically drank excessive amounts of water even after lithium therapy had been discontinued several years previously. Progressive polyuria (>6 L/d) with a urine osmolality of 190 mosm/kg H₂O developed post-operatively, and there was no change in urine osmolality after administration of exogenous vasopressin. High infusion rates of 5% dextrose in H₂O were required to prevent a progressive water deficit and subsequent hyponatremia. Due to a prolonged ileus, TPN was initiated (providing ~ 350g/L of dextrose). Subsequently, the patient developed glycosuria with a blood glucose of 572 mg/dL. Intravenous insulin was administered. The patient's urine output further increased reaching levels as high as 10 L/day. Despite progressive increases in the insulin infusion rate (up to 100 U/hr), hyperglycemia and glycosuria persisted. At this time, calculation of the patient's glucose intake revealed he was receiving ~6.95 mg/kg/min, a value which surpasses normal maximal human glucose utilization, reported to be ~5 mg/kg/min. After changing the patient's intravenous fluids to 0.25% NS to prevent negative water balance and hyponatremia, and decreasing the TPN dextrose concentration by 10%, the calculated glucose administration was decreased to ~ 3.1 mg/kg/min. This resulted in normalization of the patient's blood glucose and discontinuation of the insulin infusion within 24 hr.

Conclusions: The requirement for extreme amounts of glucose resulted in an iatrogenic hyperglycemic hyperinsulinemic state, which mimicked severe insulin resistance. 0.25% NS can be safely used, despite the small risk of cell lysis.

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THE "NON" WHOOPING COUGH

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Case Report: A 10 month old boy presented to an outlying facility with fever and cough for 1 week and was admitted with bilateral pneumonia. On the next day, he had an increased supplemental oxygen requirement prompting his referral to our hospital. He has a past history of asthma, pneumonia twice in the last 3 months, and developmental delay (DD). No history of contact with animals. Patient received only one set of vaccinations and has a history of tobacco smoke exposure.

Exam showed a fussy febrile child in respiratory distress. Lung exam revealed bilateral crackles and wheezes. Neurological exam showed global DD. The remainder of the exam was normal.

Hospital Course: He was started on ceftriaxone IV, albuterol, solumedrol IV. CXR showed bilateral perihilar and upper lobe infiltrates and cardiomegaly. Echo was done and showed a moderate size ASD measuring

7-8 mm. On day 3, he developed symptoms of CHF and started on digoxin and furosemide. He continued to have persistent fever and was transferred to the PICU secondary to worsening respiratory status, intubated and ventilated. Bronchoscopy was performed and *Bordetella bronchiseptica* was isolated from the bronchial washing and ET culture. Other lab findings include WBC 15,900 with 54% seg, 36% lymphocytes. RSV and sweat chloride tests were negative. CH50, immunoglobulin levels and neutrophil oxidative burst test were all normal. He was treated with azithromycin for 5 days based on sensitivities with improved respiratory status and resolution of fever. Patient was transferred to a cardiac center for ASD closure.

B. bronchiseptica is recognized as a respiratory tract pathogen in animals and rarely seen as a pathogen in humans. Krepler and Flamm first described it in humans in 1958. This infection occurs mainly in immunodeficient patients. A history of exposure to animals is often present but is not always identifiable. The clinical manifestations include sinusitis, tracheobronchitis, whooping cough-like illness and pneumonia. There are no definitive radiographic features associated with its pulmonary infections. This 10 month old boy did not have a history of immunodeficiency or contact with animals and therefore is unusual. While optimal therapy has not yet been determined, susceptibility testing allows appropriate antimicrobial therapy and in our patient succeeded in curing his symptoms.

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ABDOMINAL WALL HEMATOMA FOLLOWING PARACENTESIS

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Case Report: Paracentesis is a common procedure for patients with ascites. However, in a small subset of patients who do develop bleeding complications, the procedure can be devastating. We report a case of a patient who had an ultrasound guided paracentesis for ascites with devastating consequences and review the literature.

A 67 year old woman with ascites secondary to cirrhosis, an INR of 1.38 and platelets of 37, underwent an ultrasound guided paracentesis in the right lower quadrant. No immediate complications were reported but the patient was noted to have a swelling at the paracentesis site few hours after the procedure. This swelling progressively enlarged and by the next morning, the patient had developed a 24 cm × 12 cm tense abdominal wall hematoma extending from the rib cage to the inguinal ligament. The patient was transfused eight units of packed red blood cells and multiple units of platelets and fresh frozen plasma because of the enlarging hematoma, hypotension, tachycardia, pallor and anemia. A diagnosis of abdominal wall hematoma was made on a CT scan of the abdomen and a surgical consultation was requested for draining the hematoma. Intra-operatively the hematoma was seen extending anterior to and into the rectus sheath all the way from the subcostal margin to the inguinal ligament. Arterial bleeding was not seen and some venous oozing was controlled with electrocautery. The patient tolerated the surgery well but eventually succumbed to a nosocomial pneumonia.

Discussion: Paracentesis is considered a safe procedure even in patients with a coagulopathy. Hemorrhagic complications occur in less than 1% of cases and major hemorrhagic complications requiring transfusions are even rarer. Post procedure bleeding can take the form of intraperitoneal bleeding, inferior epigastric artery pseudo-aneurysm and abdominal wall hematoma, as was the case in our patient. Bleeding during the procedure can result from puncture of superficial epigastric vessels, intra abdominal collaterals or paraumbilical veins. Performing the procedure in the avascular midline under ultrasound guidance can potentially decrease these hemorrhagic complications. Coagulopathy, if present, must be corrected in addition to definitive treatment, which includes surgical drainage of abdominal wall hematomas and embolization of inferior epigastric pseudoaneurysms.

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IATROGENIC RUPTURE OF RENAL FORNIX - A CASE REPORT

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Case Report: Posterior urethral valves (PUV) is the most common cause of bladder obstruction in neonates. Presentation may vary depending upon the degree of obstruction. The development of renal insufficiency in patients with PUV is attributed to the high pressure generated by urethral obstruction. Voiding cystourethrogram (VCUG) is the investigation of choice for diagnosis. Rupture of fornix is an extremely rare complication of VCUG.

Case Presentation: We present a case of 37 week male infant prenatally diagnosed with bilateral hydronephrosis. Initial exam revealed palpable bladder and poor urinary stream during voiding. Renal ultrasound after birth confirmed the diagnosis of bilateral hydronephrosis with fluid collection in the perinephric space. VCUG demonstrated a significant ureteral and pelvicalyceal dilatation and extravasation of contrast in the right perinephric space. Shortly after the VCUG, patient was noticed to have an increase in abdominal girth. Abdominal CT scan confirmed extravasation of contrast material into the peri-renal and peritoneal spaces. The serum creatinine increased from 0.9 to 1.7mg/dl. Foley's catheter was placed allowing large amounts of mixed urine and contrast material to be drained. Later vesicostomy was performed. Eventually abdominal girth decreased and renal function improved. The infant was discharged in 2 weeks.

Discussion: Obstruction in the renal tract results in increased hydrostatic pressure and dilation of the collecting system. Decompression of the obstructed system may occur by rupture of the renal calyx at its fornix. Extravasation is usually associated with acute obstruction and occurs as the result of increased hydrostatic pressure that creates a sinus through parenchyma and capsule. This encapsulated extra pelvicalyceal collection of urine is called urinoma which has the tendency to rupture with subsequent drainage of the urine into the peritoneal cavity which can be readily seen radiographically. Urinoma formation may be seen in 3%-17% of neonates with PUV and in neonatal UPJ obstruction. In our case the iatrogenic rupture of fornix (FR) during VCUG was due to the rapid increase in hydrostatic pressure in the already dilated calyces. Management of FR involves elimination of the obstruction. FR may be avoided by emptying the bladder before the procedure.

551 IS HYPERURICEMIA (HU) AN INDEPENDENT CARDIOVASCULAR RISK FACTOR IN SPONDYLOARTHROPATHIES (SpA)?

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Purpose of Study: To determine the association and potential mechanisms of HU in a cohort of SpA patients and if treatment plays any role.

Methods Used: 30 adults SpA patients, 18/30 (60 %) Psoriatic Arthritis (PsA), 12/30 (40%) Ankylosing Spondylitis (AS). Mean age PsA 49.6 (11.0), AS 51.6 (13.2) years. Systolic (SBP) and diastolic (DBP) blood pressure and body mass index (BMI) were assessed. A quantitative ELISA assay for IL-6, sIL-6 R, IFN $\alpha/\beta/\gamma$, TNF α , sTNF R I/II, IL-1, IL-17, IL-23, IL-12, Fasting glucose, and lipid profile, Apolipoprotein B/A1, uric acid, CRP and ESR were done. Hyperuricemia was defined as ≥ 6 mg/dl. Metabolic Syndrome was defined according to the American Heart Association and National Heart, Lung and Blood Institute. Regression models, chi-square tests, and two-sample t-tests were used to examine the influence of diseases, treatments and UA category on clinical and serological biomarkers.

Summary of Results: Of the 30 patients 14 (46.7%) had UA levels ≥ 6 mg/dl. HU was present in 57.9% of PsA and 27.3% of AS. UA levels were significantly higher for PsA patients ($p=0.009$) and naive patients ($p=0.019$). PsA naive subjects had significantly higher mean UA levels than PsA TNF ($p=0.025$) and AS DMARD ($p=0.004$). SpA had metabolic syndrome that was independent of treatment ($p=0.034$); and significantly lower VEGF levels ($p=0.039$). In SpA HU the mean SPB was significantly higher ($p=0.049$). For SpA naive HU, DBP was significantly higher ($p=0.043$), and VEGF was significantly lower ($p=0.020$) than patients in other treatments. TNF HU had significantly lower mean HDL ($p=0.049$).

Conclusions: HU is an independent risk factor in SpA, present in almost half of the studied population, mainly among PsA patients. HU was associated with HTN, low HDL, adiponectin and VEGF levels. These findings have implications in the pathogenesis of CVD (ATE) and support the rationale for early treatment of HU in chronic inflammatory conditions.

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TNF-ALPHA BLOCKADE INDUCED HEPATIC SARCOIDOSIS IN PSORIATIC ARTHRITIS (PsA)

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Purpose of Study: To study the cytokine profile in a 52 year old woman with psoriasis, PsA, and hepatitis C (HCV) who developed hepatic sarcoidosis following Etanercept therapy for 7 months.

Methods Used: The subject's biomarkers levels were compared to the biomarkers level of 5 healthy controls and separately to 11 PsA patients on TNF blockers- 8/11 PsA patients were on etanercept. PsA mean disease and treatment duration were 158.4 (114.5) and 72.1 (42.1) months respectively. TNF- α , sTNF RI/RII, IFN- $\alpha/\beta/\gamma$, IL-1 α , IL-17, IL-6, IL-15, IL-7, Adiponectin, Leptin, EGF, VEGF, sIL-1 R, sIL-6 R, IL-12, IL-23, and IL-17 were assessed by ELISA. Royston's approximation of the Shapiro-Wilk test, Tukey's method, Shapiro-Wilk test was applied as implemented in PROC UNIVARIATE in SAS version 9.1 (SAS Institute Inc., Cary, NC) and Grubbs test were used.

Summary of Results: All PsA and controls tested negative for TB (Quantiferon), hepatitis B/C, HIV, ACE level, chest x-ray, liver function test (LFTs). LFTs from the affected subject became elevated after 3 months of Etanercept therapy maintaining a stable viral load since Oct 2007, after 45 days of stopping Etanercept LFT's normalized. Abdomen, pelvis and chest CT scans showed splenomegaly. Liver biopsy showed granulomatous hepatitis. Serologic biomarkers of the subject in comparison to the controls indicate that both sTNF RI ($p<0.001$) and IL-1 α values were higher when compared to the 11 PsA patients on TNF blockers.

Conclusions: The clinical course, increased levels of sTNF RI and IL-1 α in the subject as compared to the other PsA on TNF blockade and controls, in addition to recent reports of granulomatous reactions associated with TNF blockade suggest that Etanercept-induced inflammatory cytokine imbalance played an important role in the observed hepatic sarcoidosis.

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A RARE CASE OF DEXTROCARDIA, SITUS INVERSUS, ATRIOVENTRICULAR AND VENTRICULOARTERIAL DISCORDANCE AND RIGHT ANTERIOR AORTA

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Case Report: BACKGROUND- Dextrocardia is associated with multiple and complex congenital cardiac anomalies. In situs inversus with dextrocardia, the majority have concordant AV and VA connections. The presence of discordant AV and VA connections is extremely rare. Only three cases have been reported in literature with findings similar to our case. CASE DESCRIPTION- Patient had a prenatal diagnosis of complex heart disease with L transposition, PS and VSD as seen on a fetal echo. It was a twin delivery at 29 weeks gestation and the other twin was healthy. Birth was uncomplicated with APGARs 8 and 9. The only symptom on first day of life was apnea. On examination patient was acyanotic and had a 1/6 SEM at right upper sternal border. Pulses were 2+ in all extremities and abdomen was soft with no hepatosplenomegaly. SpO2 on presentation was 96%. CXR showed situs inversus, dextrocardia and normal pulmonary markings. An echocardiogram showed dextrocardia with visceral and atrial situs inversus along with AV discordance, VA discordance, right anterior aorta, subvalvular PS and VSD. In the next few days patient developed increasing cyanosis and was referred for possible modified Blalock Taussig shunt. Surgical intervention was deferred as the cyanosis improved. The patient has been doing well with conservative management until recently when increased cyanosis was seen. A diagnostic catheterization revealed findings consistent with her echo. The patient is now 2 years old and is scheduled for a biventricular repair. DISCUSSION- The case is an example of situs inversus, dextrocardia with AV and VA discordance and right anterior aorta. This is an inverted form of corrected TGA. Although the segmental cardiac connection would theoretically be physiologically correct, the associated anomalies in the previous all reported cases were severe, resulting in profound hemodynamic impairment. Our patient has been managed conservatively until 2 years of age. CONCLUSION- Dextrocardia, situs inversus with AV and VA discordance along with right anterior aorta is an extremely rare finding. To the best of our

knowledge this is the fourth such case reported and our case differed in the severity of hemodynamic impairment.

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DRAMATIC IMPROVEMENT IN DIABETES CONTROL WITH A "MIRACLE" INSULIN

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Case Report: A 65 year old male patient with refractory type II Diabetes Mellitus (DM), was referred to the endocrinology clinic for further management. His DM was diagnosed 30 years ago and had been on insulin for 5 years. Several traditional insulin regimens failed to achieve a good control, including NPH and glargine. At presentation, 430 total units of insulin per day was in use (NPH + aspart) without success. PMH: morbid obesity (BMI 59.79), COPD, poorly treated sleep apnea, pulmonary hypertension, congestive heart failure, hypertension and hyperlipidemia. ROS: weakness, somnolence and depression. Unremarkable family and social history. Medications: pramlintide, aspirin, atenolol, gabapentin, gemfibrozil, losartan, nifedipine, risperidone, simvastatin, spironolactone, trazodone, and venlafaxine. PE: normal vital signs, positive for acanthosis nigricans in the groin area and bilateral ankle pitting edema. Laboratory: HbA1c 10.4 and 9.3 (last 6 months), positive anti-insulin antibodies of 5.7 (nl < 1), baseline Cr 1.3, and normal 24h urine cortisol. The patient was diagnosed with severe insulin resistance and started on 100 units of U-500 insulin TID + SSI. Few weeks later, patient reported significant improvement in glycemic control and much less SSI requirement. The HbA1c reached 7.2 within few months, something he had not seen for several years. He was highly satisfied calling this the "miracle insulin".

Discussion: U-500 is 5 times concentrated form of insulin, indicated in cases of severe insulin resistance (requiring > 200 units/day). U-500 is regular insulin but possess NPH like activity, been suitable for basal. The reduced injected volume increases the compliance (less pain and pricks) and enhances consistent insulin delivery. Its use has showed to decrease the HbA1c in 1.6%. U-500 has been available in The United States since 1982 but its use remains suboptimal. Given the increasing prevalence of morbid obesity and associated complications like sleep apnea, we anticipate U-500 insulin offers an invaluable option in patients with marked insulin resistance and should be considered early in the management. U-500 is also a cost effective modality.

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POSITIONAL VENTRICULAR TACHYCARDIA

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Case Report: A 67yo male was moved to the ICU after his nephrectomy for renal cell carcinoma. The patient had several episodes of new-onset wide complex tachycardia which was noted to occur only when he was placed on his left side and resolved when he returned to the supine position. The patient was asymptomatic and maintained his BP during the runs of tachycardia. PMH: renal cell CA, resected prostate CA, DM and neuropathy. Meds: gabapentin, oxycodone, aspirin and ondansetron. Physical exam: HR 100, BP 180/66, dull R lung base and mildly distended abdomen. Lab: electrolytes and cardiac enzymes were normal with a baseline Cr of 2.1. Telemetry showed nonsustained VT with a LBBB morphology. CXR showed a portacath with the tip of the catheter that appeared to be in the superior vena cava. However, review of a cardiac catheterization done 8 months prior revealed the catheter tip in the R ventricular apex. Echocardiogram was normal with an EF of 55% but again the catheter appeared to be in the RV apex. It was postulated that the intermittent VT was triggered by irritation of the right ventricle by the catheter tip. Interventional radiology was asked to relocate the catheter and the tachycardia disappeared completely.

Discussion: The most common cause of VT is typically ischemia, however in this case that was ruled out by negative enzymes, a normal EKG, and a fairly recent normal cath. The normal EKG and electrolytes also ruled out other causes of VT including prolonged QT interval, with motion artifact also being ruled out. Some cases of VT are caused by reentry mechanisms, increased automaticity, or by triggered activity. The LBBB pattern seen here,

which is right ventricular in origin, and the occurrence with certain positions (left side down) were both supportive of this latter possibility. This case reminds physicians to carefully evaluate the position of any central catheter in the setting of new onset wide complex tachycardia, especially when ischemia and other important etiologies have been ruled out, since repositioning of such a catheter can completely eliminate a dangerous arrhythmia.

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PULMONARY SCEDOSPORIOSIS

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Case Report: A 31 year-old female with AIDS with a CD4 count of 51 was hospitalized due to the acute onset of dyspnea. Oxygen saturation was 67% on room air and heart rate was 120 beats/minute. Physical examination was remarkable for diminished breath sounds over the left lung. Computed tomography of the chest revealed 3 cavitary lesions in the right lung and 1 in the left lower lobe. A chest tube was immediately inserted. Labs revealed a white blood cell count of 18,000 cells/mm³. Cultures of the blood for bacteria and fungi and sputum for acid-fast bacilli, serum cryptococcal antigen, urine histoplasma antigen, serum galactomannan antigen, and serum beta-D-glucan assay were negative. PPD was non-reactive. Bronchoscopy was done and cultures for bacteria, fungi, and acid-fast bacilli were negative. Due to a persistent air leak, a thoracotomy with decortication was done. Histopathology revealed necrotizing granulomas and branching hyphae suggestive of aspergillosis. Oral voriconazole at 200 mg every 12 hours was begun. Nine days after the thoracotomy, cultures of the biopsy material grew *S. apiospermum*. Three weeks later, the patient was evaluated as an outpatient and voriconazole was changed to liposomal amphotericin B at a dose of 5mg/kg IV 3 times a week to minimize potential interactions with antiretroviral medications. Antifungal susceptibilities demonstrated resistance to amphotericin but showed susceptibility to itraconazole. After obtaining these results, therapy was changed to oral itraconazole 200 mg twice daily. Opportunistic fungal pathogens, such as *Scedosporium*, have become increasingly recognized as a cause of invasive disease in immunocompromised hosts. Although an altered immune status appears to be a key factor in disease development, *scedosporiosis* has not commonly been reported in patients with HIV. Diagnosis by histopathologic methods may confuse *Scedosporium* with other pathogenic fungi in the same class such as *Aspergillus*. Septated hyphae with acute angle branching are characteristic of both fungi. Definitive diagnosis can be made with fungal culture. Establishing a definitive diagnosis is crucial to treatment because, unlike *Aspergillus*, *Scedosporium* is often resistant to amphotericin B. Treatment of *S. apiospermum* infection can be difficult due to antifungal resistance. Voriconazole has the most potent in vitro activity.

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BORDETELLA BRONCHISEPTICA BACTEREMIA IN A PATIENT WITH AIDS

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Case Report: *Bordetella bronchiseptica* is a pleomorphic gram-negative bacillus most often associated with respiratory infections in animals. Human infections are rare but can occur, particularly in immunocompromised hosts. We report a case of a 44 year-old male who presented with the acute onset of fever and chills and was found to have *B. bronchiseptica* bacteremia due to an infected hemodialysis catheter.

The patient had AIDS with an absolute CD4 lymphocyte count of 93 cells/microliter and was receiving zidovudine, tenofovir and nevirapine. Due to HIV nephropathy he had been undergoing hemodialysis via a catheter thrice weekly for 6-years. His only animal contact was a pet cat at home. On admission abnormal vital signs included a temperature of 39 °C, heart rate of 133 beats/minute, and oxygen saturation of 98% on 2 liters nasal cannula. On physical exam the left forearm appeared clean with no signs of cellulitis and the left internal jugular catheter site appeared to have no obvious signs of infection. Blood cultures obtained on admission were positive for *B. bronchiseptica*. The organism was susceptible to levofloxacin, gatifloxacin, gentamicin, imipenem and trimethoprim-sulfamethoxazole. Empiric vancomycin and gentamicin were begun on admission and then changed to ciprofloxacin and gentamicin for 2-weeks once the susceptibility pattern was

known. Repeat blood cultures drawn 12 and 26 days later and remained clear. Hemodialysis catheter was not removed since the bacteremia cleared and the patient's clinical status improved on antibiotics.

First isolated from laboratory dogs in 1910, *B. bronchiseptica* has been responsible for outbreaks of rhinitis, otitis, tracheobronchitis and pneumonia in both wild and domestic animals. The patient we described represents the first report of *B. bronchiseptica* bacteremia in a patient with AIDS. Our patient's history suggests that the likely source of infection was the hemodialysis catheter; infection may have been acquired through contact with a cat. In our case the patient's clinical status improved rapidly with the administration of appropriate antibiotics. The significance of our report illustrates the importance of unusual organisms as potential pathogens in immunocompromised individuals.

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LATE ONSET OF RESPIRATORY FAILURE IN A NEONATE WITH THE PDAC SYNDROME (PULMONARY HYPOPLASIA/AGENESIS, DIAPHRAGMATIC HERNIA/EVENTRATION, ANOPHTHALMIA/MICROPHthalmia AND CARDIAC DEFECT)

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Case Report: A 39-week female infant who was the product of a non-consanguineous pregnancy was delivered to a healthy 17-year-old gravida 1 white woman with a negative family history. The prenatal period, labor and delivery were uneventful. Initial physical exam was normal except for right anophthalmia and complete cleft palate. Chest x-ray showed right diaphragmatic eventration, right upper lobe atelectasis and right middle lobe hypoplasia with a normal left lung. Fluoroscopy showed normal excursion of the right hemidiaphragm in comparison to the left without paradoxical motion. MRI of the brain showed amorphous substance and lens in the right globe with a normal left eye. Ophthalmology examination showed coloboma of the left optic nerve and no visible structure on the right eye. Echocardiogram showed an atrial septal defect, aortic stenosis, peripheral pulmonary stenosis and a PDA at 3 days of age which was managed with intravenous ibuprofen. The baby did well on room air until day 6 when she developed acute respiratory failure. Bronchoscopy showed diffuse tracheomalacia. The infant required tracheostomy for long term ventilator support, a Nissen fundoplication and G-tube placement. The karyotype was that of a normal female (46,XX), DNA sequencing analysis showed no mutations of the STRA6, SOX2, PAX6, SIX3 or SIX6 genes. The patient was discharged on a home ventilator after 5 months. By 14 months of age the patient was off the ventilator and doing well. Discussion: Pulmonary agenesis/dysgenesis/hypoplasia, a diaphragmatic defect, microphthalmia/anophthalmia and cardiac defects constitute the PDAC syndrome (also known as Matthew-Wood Syndrome or Spear syndrome). This is a genetically heterogeneous disorder involving the genes listed above. The outcome in most cases is intrauterine death or early post-natal death due to respiratory failure and other complications. This case serves as a reminder to pediatricians to always seek associated birth defects in patients born with anophthalmia since this child may have died had she been sent home before the pulmonary and cardiac defects had become clinically evident.

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"WE WOULD, AND WE WOULD NOT": A TRAGIC CASE OF KELL

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Case Report: A 44-year-old African American woman was admitted for vaginal hysterectomy (VH) due to a four month history of menometrorrhagia despite medical management. Medical history was significant for Systemic Lupus Erythematosus, well controlled on hydroxychloroquine sulfate, and hypothyroidism. Admit vital signs were unremarkable and her pre-operative hematocrit was 30.8%. She was A positive and her coagulation panel normal; however, she was found to have an anti-Js(b) antibody. The surgical team was informed that there was no appropriately typed blood in the hospital inventory. Due to the urgency of the patient's condition a VH was performed without any initial complications. Post-operatively, she decompensated and hematocrit decreased to 19.3%. Exploratory laparotomy showed extensive bleeding from

the surgical sites. A left oophorectomy and bilateral hypogastric artery ligation was performed. Due to extensive blood loss and critical status, she was resuscitated with products including 12 units Js(b)+ blood and monitored in the intensive care unit. Follow-up hematocrit was 40.8%.

Clinical findings and serial labs were consistent with acute hemolytic transfusion reaction (AHTR). Due to severe heme pigment-induced acute tubular necrosis, continuous renal replacement therapy was initiated but was unable to be continued due to hypotension. Further evaluation showed no signs of lupus exacerbation or disseminated intravascular coagulation. Despite receiving appropriately typed blood, her anemia worsened. On post-operative day 6, she succumbed to multisystem organ failure due to complications associated with AHTR. Js(b) is a member of the Kell system. Considered a high-frequency antigen, it is seen on RBC of nearly 100% of Caucasian and 99% of African descent individuals. Js(b)-phenotypes are not seen on RBC of Caucasians and only 1% of African descent individuals. Most adverse transfusion reactions ending in death are seen in neonates; however, adults appear to suffer from mild to moderate hemolytic anemia that resolves after supportive therapy. To our knowledge this is the first case of a Js(b)-individual receiving 12 units of Js(b)+ blood at one time who eventually died due to AHTR.

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A RARE DISORDER PRESENTING WITH UPPER GASTROINTESTINAL BLEEDING

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Case Report: Background: There are multiple causes of upper gastrointestinal bleeding in children. Esophageal varices due to portal hypertension can cause dramatic bleeding needing immediate intervention. Congenital hepatic fibrosis (CHF) is a rare congenital multisystem disorder affecting primarily the renal and hepatobiliary systems. The etiology is a ductal plate malformation affecting the small intrahepatic bile ducts and periportal fibrosis leading to portal hypertension. Aim: To report a common presentation of a rare disorder. Case Report: A 10 year old boy presented with epigastric abdominal pain and hematemesis. On examination, he was tachycardic, hypertensive, and pale. His spleen was palpated midway between his left costal margin and his pelvic brim with a prominent bulge towards the umbilicus. Laboratory tests showed WBC 5,500, hemoglobin 8.9, hematocrit 27.1, MCV 73, platelets 93,000, total protein 5.5, albumin 3.2, total bilirubin 0.7, alkaline phosphatase 116, AST 18, ALT 25, BUN 34, creatinine 0.72, and INR 1.14. Doppler ultrasound showed patent hepatic and portal veins with massive splenomegaly and bilateral, large echogenic kidneys. An upper endoscopy showed grade III-IV varices and portal hypertensive gastropathy. Esophageal variceal banding was performed. An open liver biopsy revealed broad bands of periportal and septal fibrosis with dilated and proliferated bile ductules embedded in dense fibrous connective tissue. The hepatocytes appeared normal. He subsequently had 3 more band ligation sessions and the varices decreased to grade I-II. He has had no further bleeding. The family was screened by renal ultrasound. Discussion: CHF and autosomal recessive polycystic kidney disease can present at birth with oligohydramnios, or later in life with portal hypertension. It is a progressive disease that can require renal transplantation or portosystemic shunt. Upper gastrointestinal bleeding can be life-threatening. Band ligation of esophageal varices and beta-blockers can be utilized to prevent bleeding and postpone the need for surgical portosystemic shunt. Since it is an inherited disease, it is important to screen family members.

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PERIPARTUM CARDIOMYOPATHY

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Case Report: A 29-year-old Gravida4 Para3 African American woman with a history of childhood asthma and hypertension presented to the hospital two weeks after she had her 3rd child, via C-section, with 2 days of progressive shortness of breath, moderate clear-yellow sputum production, and subjective fevers. The patient also reported 1 day of left calf tenderness and swelling. Upon initial assessment the patient was moderately hypertensive and had a body mass index of 42.1. On physical examination, she had a jugular venous pressure of 8cm, tachycardia and bibasilar crackles. Serum chemistries demonstrated anemia and a respiratory alkalosis with an A-a gradient of 55. Further lab studies revealed an unremarkable white blood cell count, urine

toxicology screen, and comprehensive metabolic profile. An EKG showed tachycardia, left axis deviation and left atrial enlargement. Chest radiograph showed cardiomegaly and bilateral airspace disease. A chest cat scan with pulmonary embolus protocol showed no filling defects. The patient was treated for pneumonia and a 2D echocardiogram showed an ejection fraction of 30-35% with left ventricular and atrial enlargement. The patient was diuresed with lasix, the antibiotics were stopped and her shortness of breath began to subside. The patient was discharged in good condition on lisinopril, carvedilol, a low sodium diet with fluid restriction, and further cardiology follow-up.

Peripartum cardiomyopathy is an uncommon form of congestive heart failure occurring in one out of every 3000 to 15,000 pregnancies. Women at higher risk for developing peripartum cardiomyopathy are greater than 30 years of age, African American, multiparous, and those with twin births. The criteria for the diagnosis of peripartum cardiomyopathy includes left ventricular dysfunction with an ejection fraction <45% of unknown etiology and manifestation of heart failure symptoms during the last month of pregnancy or within 5 months of the delivery. The treatment for peripartum cardiomyopathy is similar to that for other nonischemic dilated cardiomyopathies with due consideration given for the fetus. Angiotensin converting enzyme inhibitors are contraindicated during pregnancy and can only be used in the post-partum period.

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HOSPICE OR HOPE IN A PATIENT WITH END-STAGE METASTATIC NEUROENDOCRINE CARCINOMA?

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Case Report: A 58 year old woman with metastatic pancreatic neuroendocrine carcinoma diagnosed in 1991, presented in March 2006 with anorexia, increased cold sensitivity, fatigue, pedal edema, alternating periods of diarrhea and constipation and significant weight loss despite adequate calorie intake over 6 months. Physical exam revealed massive hepatomegaly and a grade 3/6 holo-systolic murmur. Despite maximal medical management including octreotide therapy, the patient's condition deteriorated and she was referred to hospice in July 2006. Three months later, thyroid function tests were obtained and demonstrated hyperthyroidism. Endocrine consult confirmed lid lag and a goiter. Propylthiouracil followed by I-131 radioablation and levothyroxine titration resulted in resolution of symptoms. The patient's health returned to the level prior to the onset of thyroid storm over nine months, she was discharged from hospice in September 2007, and continues to thrive.

Thyroid storm, a disorder with variable presentations, is marked by sudden, life-threatening symptoms like fever, tachycardia, tremor, nausea, vomiting, diarrhea, dehydration, delirium, and coma. Other manifestations include hypertension, weight loss, and multiple organ dysfunction. Common causes for thyroid storm include trauma, infection, radioactive iodine therapy, external radiation treatments, and discontinued use of hyperthyroid medications. Thyroid carcinoma is an uncommon cause of thyrotoxicosis. Serum chemistries that support the diagnosis of thyroid storm include an elevated free T4, decreased TSH, and elevated liver enzymes.

Our patient presented with signs and symptoms of end-stage malignancy, including weight loss. After hospice referral, hyperthyroidism was diagnosed and successfully managed. Recognizing and treating potentially independent and reversible conditions in the end-stage cancer patient may lead to a longer survival and improved quality of life. Etiology of her hyperthyroid state remains unclear but not related to either the underlying malignancy or its treatment.

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EOSINOPHILIA: PARASITES, ALLERGIES, LEUKEMIA... LARGE CELL CARCINOMA?

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Case Report: A 64 year old woman with no significant past medical history presented to the emergency department complaining of back pain for 3 months and shortness of breath for 4 days. The patient reported a cough productive of reddish sputum about six days prior to presentation. Upon further questioning, she also admitted to multiple episodes of cough with reddish sputum within the last year. However, she had never sought medical care for this issue. The patient also reported a 10 pound weight loss in the past

week. Physical examination was significant for bronchial breath sounds on the right. Egophany and crackles were also appreciated throughout the right lung. Laboratory data upon presentation included a white blood cell count of 20,000/ μ L with the following differential: 48% segmented neutrophils (9,600/ μ L), 7% bands (1,400/ μ L), 11% lymphocytes (2,200/ μ L), 7% monocytes (1,400/ μ L), 26% eosinophils (5,200/ μ L), and 1% myelocytes (200/ μ L). Initial chest x-ray showed total atelectasis of the right lung secondary to a mass obstructing the right main bronchus. Ultimately, the patient was diagnosed with non-small cell carcinoma (Large Cell) via bronchoscopy and biopsy of the mass.

The presence of eosinophilia is typically associated with a differential diagnosis that includes allergic reactions, parasitic infestations, certain forms of vasculitis, or leukemic processes. Although not usually associated, it has been reported to be present with certain types of solid tumors including thyroid, hepatocellular, breast, and lung cancers. In regards to lung cancers eosinophilia has been reported in cases of adenocarcinoma, small cell, and squamous cell carcinoma. However, it has been rarely reported to be present in large cell carcinoma. Factors that have been hypothesized to be involved in the production of the eosinophilia includes GM-CSF, G-CSF, and IL-5. The presence of eosinophilia has also been suggested to be associated with a worse prognosis.

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RHEUMATOID ARTHRITIS OF THE ROBUST REACTION TYPE

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Case Report: A 61 year-old white male presented with many year history of prolonged AM stiffness, polyarthritis of hands and wrists as well as nodules on extensor surface of upper extremities. The symptoms were unresponsive to OTC NSAIDs. He had a previous CVA and 90 pack-year of smoking. His systemic examination was unremarkable. The musculoskeletal examination revealed ulnar deviation, active synovitis of multiple metacarpo-phalangeal joints (MCP) & proximal interphalangeal joints (PIP) of both hands and wrist. Multiple rheumatoid nodules were palpable at elbows. His labs showed RF



of 295 and + Anti-CCP. Severe destructive changes were present on radiographs of hands. A diagnosis of rheumatoid arthritis (RA) of arthritis robustus variant was made and patient aggressively treated with DMARDs. His hands photographs and radiographs portray these findings remarkably. Arthritis Robustus is an unusual but not that uncommon presentation of disease. Most patients are male, often with deformity with little pain and disability. Peri-articular osteopenia is unusual; whereas new bone proliferation at joint margins near significant erosions of bone and subchondral cysts are common. Most of these patients have a similar prognosis to the other presentations of RA.

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A RARE MEDIASTINAL TUMOR - CASE REPORT AND FOCUSED REVIEW OF THE LITERATURE

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Case Report: Paragangliomas are rare neuroendocrine tumors arising from the aorticosympathetic paraganalia. Mediastinal paragangliomas represent 2% of all paragangliomas and 0.5% of mediastinal tumors. Here we present a patient with a paraesophageal paraganglioma which was non secretory but caused dysphagia.

A 73 year old woman presented to her primary care provider complaining of progressively worsening difficulty in swallowing primarily to solids. She had no history of headache, vertigo, tinnitus, hypertension, or flushing. Chest CT revealed a large paraesophageal mass in the posterior mediastinum superiorly. A CT guided fine needle biopsy was consistent with a paraganglioma (PG). A PET scan showed significant activity only in the superior mediastinum. The patient underwent resection of the tumor. A 5 × 4 × 2.5cm mass with a tan pink parenchyma and punctate hemorrhage was removed. developed Horner's syndrome in the immediate post operative period which resolved spontaneously. The overall post operative recovery was uneventful. Her dysphagia had completely resolved on follow-up. The patient is to be followed up for recurrence of the mass or appearance of metastatic lesions.

A review of the literature revealed about 45 reported cases of a posterior PG including those in the pediatric age group. 50% were non functional and 10% were malignant with metastasis. Posterior mediastinal PG occur in young adults mean age in the third decade with no gender predilection. Symptoms were caused either from a secretory activity of the tumor like palpitation, sweating, and hypertension or are caused by the physical presence like dysphagia. The tumor is discovered incidentally on imaging in those without secretory activity. Thoracic imaging is essential to evaluate the extent of the tumor and plan the excision. Surgery is the treatment of choice for the well-circumscribed mediastinal PG without the need for other treatment modalities.

The diagnosis of a PG is confirmed by histology and immunohistochemical staining. Once the tumor is removed a life long follow-up is mandatory as there is no reliable method to predict malignancy in these masses.

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OTO - PALATO - DIGITAL SYNDROME TYPE II IN A MALE INFANT WITH TWO HEMIZYGUS MISSENSE MUTATIONS IN THE FLNA GENE INHERITED FROM THE MOTHER

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Case Report: We report a male infant with typical clinical and radiological features of oto-palato-digital syndrome type II (OPD II) with a novel mutation unreported before. The dysmorphic features noted at birth include brachycephaly, large anterior fontanel, frontal bossing, low set ears, hypertelorism, down slanting palpebral fissures, midfacial hypoplasia, small mouth, micrognathia and cleft palate. He also had small thorax, omphalocele, cryptorchidism and inguinal hernia. Extremities revealed bowing of the long bones and joints showed limited range of movements with flexion deformity. Hands and feet showed multiple deformities consistent with OPD II. Radiological survey confirmed all the skeletal deformities including the absence of fibulae which are characteristic of OPD II. Hearing screening identified conductive deafness. Karyotype revealed normal XY. DNA testing identified two hemizygous missense point mutations in the FLNA gene which encodes for the protein filamin A. The mutation c.613T>C (p.Cys-205-Arg) is a novel mutation un-

reported previously, while mutation c.5290G>A (p.ala-1764-Thr) is a sequence variation that has been previously reported in an adult female with X-linked periventricular heterotopia (another genetic condition caused by mutations in the same FLNA gene). However our patient did not show periventricular heterotopia in the brain both by imaging as well as at autopsy. Mother did not have clinical manifestations and screening for mutations in the FLNA gene revealed the same 2 mutations, further confirming the X-linked dominant mode of inheritance. So far about 45 cases of OPD II have been reported in the literature. But only in few cases the mutations have been mapped. The presence of bowing of the long bones, absent fibulae and abnormal digits in the prenatal scans should alert the possibility of OPD II. The mother of our patient received poor antenatal care and this condition was not diagnosed before birth. Death in early infancy is typical of OPD II in boys and our patient died at the age of 3 months from respiratory failure.

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FULMINANT HEPATIC FAILURE FROM ACCIDENTAL ACETAMINOPHEN OVERDOSE COMPLICATED BY CHRONIC ALCOHOL CONSUMPTION

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Case Report: A 41-year old man with a history of ethanol abuse presented to the emergency department with abdominal pain, dyspnea, headache, nausea, and vomiting two days after drinking 32 ounces of bourbon. For an undetermined time, the patient ingested at least six Tylenol #3 tablets daily. Upon admission, he was responsive, tachycardic, hypoxic, and hypothermic. Physical exam revealed scleral icterus, conjunctival hemorrhages, petechiae over the thorax, and diffuse abdominal tenderness. Initial chemistries revealed an elevated total bilirubin (24.9mg/dL), AST (22,930U/L), ALT (12,900U/L), ammonia level (94mmol/L), and decreased platelet count (6,000). He had an elevated prothrombin time (45.8sec), partial thromboplastin time (36.5sec), and INR (4.0). He was in renal failure with a BUN of 44mg/dL and creatinine of 5.86mg/dL. The serum acetaminophen level was less than 10 but he received N-acetylcysteine because of his chronic acetaminophen usage. His liver function tests trended downward. The patient's HIV, viral hepatitis panel, ceruloplasmin were all negative. He received multiple blood product transfusions with minimal improvement. Renal function continued to worsen. Lactulose was initiated secondary to increasing ammonia levels and encephalopathy. On the third day of admission he became severely bradycardic and expired. Autopsy revealed massive hepatic necrosis.

Fulminant hepatic failure (FHF) manifests with encephalopathy, coagulopathy, jaundice, and multiorgan failure. FHF has a mortality rate greater than 80%. Acetaminophen toxicity is the most common cause of FHF and is more significant among chronic alcohol users. Chronic alcohol use depletes hepatic glutathione stores preventing breakdown of N-acetyl-p-benzoquinoneimine (NAPQI), a toxic metabolite of P450 metabolism of acetaminophen. Malnutrition also depletes hepatic glutathione levels. Massive hepatic necrosis is a hallmark pathological finding in acetaminophen toxicity. Patients often have undetectable serum levels of acetaminophen (<10mg/L) when associated with accidental, chronic overdoses. Acetaminophen toxicity should be considered in alcoholics with chronic acetaminophen use, even if their acetaminophen levels are less than 10mg/L.

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TROPICAL PULMONARY EOSINOPHILIA: A COMMONLY UNDER DIAGNOSED CAUSE OF CHRONIC COUGH IN IMMIGRANTS

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Case Report: Tropical Pulmonary Eosinophilia (TPE) is a common cause of chronic cough in tropical countries where parasitic infections are still prevalent. TPE is increasingly seen in people who migrated to the USA from endemic countries.

A 28-year old student was referred by his primary care physician to the allergy clinic with a 4 month history of cough and dyspnea on exertion preceded by clear rhinorrhea and nasal congestion. Although the rhinorrhea and congestion resolved after 2 weeks, the cough gradually worsened over the next 8 weeks with nocturnal wheezing and post-tussive emesis. The cough

and dyspnea on exertion were refractory to guaifenesin, mucinex, dextromethorphan, hydrocodone, nasal fluticasone spray, and albuterol inhaler. He denied fever, chest pain, or headaches. His travel history included a 4-week stay in a rural village in south India 2 months prior to the onset of symptoms. His past medical history was significant for 2 episodes of filarial epididymo-orchitis. He denied smoking, use of illicit drugs or alcohol abuse. Vital signs and physical exam were unremarkable except for occasional wheezes and cough upon deep inspiration. Labs were significant for WBC55,000/mm³, eosinophils 30,000/mm³, IgE-3000 IU/ml. Anti-filarial IgG and IgE antibodies were positive at high titers. Anti-strongyloid antibodies were weakly positive. Ascaris IgE and Aspergillus Ig/ml were negative. Chest cat scan revealed mild peripheral interstitial thickening at the bases bilaterally. The patient was diagnosed with TPE and successfully treated with diethylcarbamazine (DEC) 2mg/kg/dose three times a day for 3 weeks.

Tropical pulmonary eosinophilia (TPE) is a hypersensitivity reaction to filarial worms namely *Wuchereria bancrofti* and *Brugia malayi*. Pulmonary involvement is the hallmark for this condition. It is usually characterized by pentad of chronic paroxysmal nocturnal cough, wheezing, shortness of breath, elevated serum IgE (>1,000 IU/ml), and peripheral eosinophilia (>3,000/mm³). The detection of high titers of anti filarial IgE and IgG antibodies, favorable response to DEC treatment, and the absence of microfilaria in the blood confirm the diagnosis.

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RHABDOMYOLYSIS IN A PATIENT WITH POLYMYOSITIS SECONDARY TO HEPATITIS C

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Case Report: A 45-year-old Afro-American incarcerated man with history of intravenous drug abuse, hepatitis C, and rheumatic fever presented with a 4 week history of progressive weakness in all his extremities. He also had difficulty in standing up from a sitting position and was unable to raise arms above shoulder, or lift objects. He denied fevers, cough, headaches, or diarrhea. On review of systems he claimed to have difficulty swallowing solid foods, chest pain, mild shortness of breath, and weight loss. He had 20 pack year smoking history, used alcohol, cocaine, and heroin. Physical exam was significant for tenderness in both thighs. He had 3/5 muscle strength in all extremities with weakness more pronounced in the proximal muscle groups. He had good hand grip. Deep tendon reflexes were 1+. He had no rash or Gottrohn patches. Lab studies revealed iron deficiency anemia and mild transaminitis. He had a normal urine toxicology screen, ANA screen, TSH, and serum creatinine. Urine analysis showed blood but no erythrocytes. His initial creatinine phosphokinase (CK) was 26,250 U/L. The initial serum aldolase was low at 1.1 U/L but increased to 9.0 U/L in 10 days. Rheumatoid factor was high at 144.9 IU/ML, and the ENA 6 screen was negative. MRI of both lower extremities showed symmetric intermuscular and intramuscular edema in deep compartments of both legs.

Rheumatology was consulted and the patient was diagnosed with polymyositis with associated rhabdomyolysis secondary to hepatitis C. The patient was started on aggressive intravenous fluid resuscitation and his CK level fell to 4,000 U/L in two weeks. He was started on prednisone 80 mg per day and his weakness and dysphagia slowly improved over 3 weeks.

Polymyositis is an idiopathic inflammatory myopathy that causes symmetric proximal muscle weakness, elevated skeletal muscle enzyme levels, and characteristic electromyography and muscle biopsy findings. Dysphagia is seen in 30% of cases. Polymyositis is more common in Blacks. Usually, polymyositis has a gradual progression over a period of 3-6 months, and rarely presents as an acute episode. Polymyositis presenting as rhabdomyolysis is rare. The kidneys are generally spared in polymyositis and renal failure is rare.

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VOCAL CORD DYSFUNCTION A MASQUERADER OF ASTHMA

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Case Report: Background: It's now recognized that one of the causes of "Pseudoasthma" is the Vocal Cord dysfunction (VCD) characterized by involuntary adduction of the anterior 2/3 of the vocal cord leading to dyspnea, dysphonia and wheezing often misdiagnosed as bronchial asthma. Failure to

recognize this can lead to high dose steroid therapy with its side effects during long term treatment and unnecessary intubation in the acute phase of the disease. VCD must be considered while evaluating a patient with asthma refractory to steroid therapy. **Case Report:** A 47 year schizophrenic man with Asthma was admitted with exacerbation of asthma. Though his asthma prior to this episode was labeled as mild intermittent he had required to be intubated for acute asthma exacerbation 4 times in last 10 years. During this admission in spite of high dose steroid treatment and frequent β_2 agonist nebulizations the patient experienced sudden episodes of acute cough, hoarseness of voice, dysphonia and wheezing which was slow to improve on albuterol nebulization. A flow volume loop revealed inspiratory flow limitation with flattening of the inspiratory loop indicative of variable extra thoracic upper airway obstruction all of which was suggestive of VCD. Fibro optic laryngoscopy revealed a normal appearing larynx without vocal cord dysfunction at time of examination. Patient was taught Vocal cord relaxation exercises with significant relief of symptoms. **Conclusion:** A high index of suspicion is necessary to differentiate VCD from asthma. Sudden onset of cough, dyspnea, wheezing often with hoarseness of voice without immediate relief with bronchodilators and lack of response to steroid therapy are clues to the diagnosis. A background of psychosis or sexual or physical abuse and anxiety state are often noted. This disorder may represent a conversion reaction. GERD, post nasal drip and exercise are precipitating factors as in asthma. Definitive diagnosis is made by flexible fibro optic rhinolaryngoscopy when it reveals that the anterior 2/3 of the cords adduct during inspiration while only a posterior glottic chink remains open for ventilation leading to features of upper airway obstruction. Heliox inhalation may interrupt an acute episode of vocal cord dysfunction and avoid intubation. Long term treatment involves speech therapy and vocal cord relaxing maneuvers.

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THE ABSCESS BEHIND THE CHILLS

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Case Report: A 62 years-old Caucasian male presented with severe recurrent intermittent chills for the past 3 months associated with muscle aches. Along with Rheumatoid Arthritis, he had history of bradycardia years ago for which a pacemaker was placed. This was removed due to MRSA infection, leaving the pacemaker leads behind. Physical examination revealed bradycardia and systolic murmur in pulmonary area. He had transient leukocytosis associated with episodes of chills and had thrombocytopenia. Chest X-Ray and CT of Abdomen revealed retained pacer leads with atrial lead migrating into the right hepatic vein. Transesophageal Echocardiography revealed right atrial echodense mass. It took multiple blood cultures before one set was positive for Coagulase Negative Staphylococcus. He was started on intravenous Nafcillin and Daptomycin. Warfarin was started for a possible right atrial clot. He eventually underwent median sternotomy revealing a right atrial abscess on the right atrial valve which was drained and the leads were removed. He was discharged on Clindamycin, Rifampin and Trimethoprim/Sulfamethoxazole. Many a times, pacemaker leads are left within the heart but not without complications. In one study, 51% of the patients with retained leads had complications including septicemia, superior vena cava syndrome, thrombosis, fracture of the lead, migration to pulmonary artery or hepatic vein. Higher complication rates occur with multiple abandoned pacemaker leads, multiple procedures and a younger age at initial pacemaker implantation. Commonest agent is Staphylococcus epidermidis, followed by Staphylococcus aureus. Abscess formation at the pacemaker lead implantation site years after the initial procedure is very uncommon. Removal of leads can be done by minimal invasive techniques (like Laser Sheaths, electrosurgical dissection) or median sternotomy. Abandoned pacemaker leads can be a potential source of infection even years after its placement and may present atypically with intermittent chills. Surgical option of median sternotomy should always be considered given the possibility of abscess formation.

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LYMPHOMATOUS INFILTRATION CAUSING ACUTE RENAL FAILURE IN CHRONIC LYMPHOCYTIC LEUKEMIA

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Case Report: Leukemic infiltration of the kidneys is a common occurrence in chronic lymphocytic leukemia (CLL). However, it is an extremely rare cause of renal failure. A 49-year-old man, initially diagnosed with Chronic Lymphocytic Leukemia (CLL), was found to have decreased renal function (creatinine of 2.3mg/dl) during a routine clinic visit 1 year after his diagnosis of CLL. The patient had been followed by an oncologist since the diagnosis of CLL without any treatment as his symptoms were minimal at that time. The patient was seen in nephrology clinic a month later at which time the patient's creatinine was 3.4 mg/dl. The patient began to experience night sweats and develop bulky bilateral cervical lymphadenopathy around the same time. He did not have any flank pain, or changes in his urination pattern. Initial work up for his renal failure did not reveal the cause, thus, the patient underwent renal biopsy. The patient's serum creatinine continued to rise to 5.3 mg/dl post biopsy and he was admitted to the hospital for worsening renal function. The patient's renal function continued to decline with a maximum creatinine of 7 mg/dl, however, he was still producing adequate amount of urine and did not show any symptoms of uremia. Renal biopsy revealed dense interstitial inflammation comprised predominantly of mature lymphocytes. Under the recommendations of both nephrology and oncology, chemotherapy was started with CVP-R (Cyclophosphamide, Vincristine, Prednisone, and Rituximab). The patient received his first two cycles of chemotherapy and his last creatinine was 2.3 mg/dl. The therapeutic plan was to continue with chemotherapy until the patient's renal function returned to baseline.

Direct renal involvement by CLL is frequently seen in autopsy studies especially in advance disease, but renal failure due to lymphomatous infiltration is extremely rare. This case illustrates a rare case of a patient with CLL who developed acute renal failure secondary to lymphomatous infiltration and responded well to chemotherapy with CVP-R.

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EVALUATION OF IN VIVO SKELETAL MUSCLE ELECTROPORATION AS A METHOD FOR THE STUDY OF SKELETAL MUSCLE ATROPHY

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Purpose of Study: Skeletal muscle atrophy is observed in different disease states, such as cancer, diabetes and congestive heart failure. Plasmid and siRNA electroporation into mouse skeletal muscle in vivo is a potential experimental strategy to study signaling pathways involved in skeletal muscle atrophy. We evaluated the efficiency of overexpression or suppression of genes in skeletal muscle and deleterious effect of electroporation on skeletal muscle cells.

Methods Used: Plasmids and siRNAs were incorporated into mouse gastrocnemius muscle via electroporation and gene expression was measured by quantitative PCR and immunoblotting.

Summary of Results: By changing the voltage of electroporation (CMV-EGFP plasmid, 25–200 V/cm), the expression of EGFP reached a plateau at 100 V/cm and showed a reduction at 200 V/cm. EGFP expression reached a plateau on day 3 of electroporation and remained constant for at least 2 weeks. By counting the EGFP-positive skeletal muscle fibers the transfection efficiency of plasmid was estimated to be approximately 30–40%. Furthermore, electroporation of plasmid encoding Igf-1 gene resulted in 5.43 ± 0.24 fold increase of Igf-1 mRNA. We also evaluated the efficiency of in vivo gene suppression by electroporating siRNAs into gastrocnemius muscle.

We electroporated different amount of siRNAs (0.05–0.5 nmol) and showed that 0.2 nmol of siRNA/gastrocnemius muscle was sufficient. The siRNAs against lamin and Nox4 caused $52 \pm 0.12\%$ and $68 \pm 0.02\%$ mRNA suppression 5 days after electroporation, and these suppression levels remained constant for at least 2 weeks.

On the other hand, we found that electroporation activated the skeletal muscle atrophy marker genes Atrogin-1 and MuRF-1 expression 1 day after electroporation (3.58 ± 0.18 fold and 7.53 ± 0.47 fold, respectively), followed by a gradual decrease to the initial level after 1 week. These data indicate that a recovery period is required for the in vivo skeletal muscle electroporation especially when analyzing skeletal muscle atrophy.

Conclusions: These data demonstrated that plasmid and siRNA electroporation to gastrocnemius muscle is feasible and useful for the study of signaling pathways mediating atrophy in skeletal muscle. However, a recovery period of at least 1 week is important to prevent the damage caused by electroporation.