

Abstracts

The following abstracts were presented by investigators at the Twenty-Second Annual Samuel Bronfman Department of Medicine, Mount Sinai School of Medicine Research Day on May 31, 2006. Most of the investigators serve in the Samuel Bronfman Department of Medicine, including those working at affiliated institutions such as the Bronx Veterans Affairs Medical Center, Bronx, NY; Elmhurst Hospital Center, Elmhurst, NY; Queens Hospital Center, Jamaica, NY; and St. Joseph's Hospital and Medical Center, Paterson, NJ. Abstracts from Queens Hospital Center and Jersey City Medical Center were presented as posters on Research Day, held on May 10, 2006 and May 24, 2006, respectively.

Mount Sinai School of Medicine

Low Viral Load Chronic Hepatitis B and Liver Histology. R. Akhtar and D. Dieterich. Department of Internal Medicine, Division of Liver Disease. Mount Sinai School of Medicine, New York, NY.

Background: Chronic hepatitis B is associated with high morbidity and mortality. Liver biopsy is recommended to assess the degree of liver damage in these patients. In hepatitis B e antigen (HBeAg)-negative patients, current guidelines advise the consideration of treatment once an elevation of alanine aminotransferase (ALT) levels greater than two times the upper limit of normal is observed, or moderate to severe hepatitis is discovered on biopsy. In our cohort, we describe the liver histology in patients with HBeAg-negative chronic hepatitis B associated with viral loads of HBV DNA less than 10^5 international units (IU) per milliliter.

Methods: A total of five HBeAg-negative patients (labeled A through E), naïve to treatment, underwent liver biopsy. The patients' charts were reviewed to assess demographics, comorbidities, alcohol use, previous hepatitis workup, and medications. The liver biopsy specimens were reviewed by the Department of Pathology and scored using a modified Histology Activity Index grading scale to describe the presence of necrosis and inflammation, and a modified staging scale to describe architectural changes, fibrosis, and cirrhosis.

Results: Patient A had mild to moderate interface hepatitis, no confluent necrosis, moderate portal inflammation, and fibrous expansion of most portal areas. At the time of biopsy, the patient's ALT was 35 units/L with a viral load of 51,400 IU/mL. Patient B had mild to moderate interface hepatitis, no confluent necrosis, mild portal inflammation, and fibrous expansion of most portal areas with occasional portal-to-portal bridging. This patient's ALT was 128 units per liter associated with a viral load of 100 IU/mL. Patient C had mild interface hepatitis, no confluent necrosis, mild portal inflammation, and fibrous expansion of only some portal areas. Patient C's ALT was 26 units per liter with a viral load of 100 IU/mL. Patient D had mild-to-moderate periseptal interface hepatitis, no confluent necrosis, moderate portal inflammation, and fibrous expansion of most portal areas with some short fibrous septa. This patient's ALT was 25 units/L with a viral load of 340 IU/mL. Finally, patient E had mild-to-moderate periportal interface hepatitis, no confluent necrosis, mild portal inflammation, and fibrous expansion of some portal areas. These findings were associated with an ALT of 18 units/L and a viral load of 19,100 IU/mL.

The viral loads of all five patients never measured above 10^5 international units (IU) per milliliter. Three of five patients (A, C, and E) had a history of alcohol use but denied current, regular drinking. In addition, all patients had normal levels of bilirubin, albumin, and prothrombin time while also testing negative for hepatitis C co-infection. Patients B and E had a history of hypertriglyceridemia now under treatment.

Conclusion: In patients with HBeAg-negative chronic hepatitis B, advanced findings on liver biopsy may exist with viral loads less than 10^5 copies/mL. Previous studies have identified patients with fibrosis despite normal liver function tests. However, liver damage with lower viral titers is not as well described. A larger cohort is needed to determine if these patients represent a substantial minority of the chronic hepatitis B patient population. It is conceivable that current treatment standards need to be modified to include patients with lower viral loads to prevent disease progression.

Prediction of Cases of Pneumocystis carinii Pneumonia (PCP) Pneumonia in Russia in the Absence of Prophylaxis. Lessons for Future Preparation. E. Alexander and J.R. Masci. Mount Sinai Medical Center, Elmhurst Hospital Center, Queens, NY.

Background: Data on patients with HIV/AIDS in Orenberg, Russia suggests a low rate of treatment with antiretroviral therapy/preventive therapy for PCP. Given this trend, we estimate the number of expected cases of PCP in Orenberg over the next two years.

Methods: Using data on a cohort of 59 patients from the American International Health Alliance partnership between Orenberg, Russia and Elmhurst, NY and prior data on incidence and prevalence of Pneumocystis in patients with HIV/AIDS in Europe, we calculated an expected prevalence of *Pneumocystis pneumonia* in Orenberg over the next 2 years.

Results: PCP is one of the most common AIDS-defining illnesses in the US and Europe. In the US, the frequency of PCP in AIDS patients is between 35 and 40%. In Europe, the prevalence of PCP in AIDS patients is 39%, with an incidence of 20.7/100 person-years. This would suggest an overall prevalence of PCP of approximately 40% in patients with AIDS, and an incidence of up to 20/100 person-years. Several studies however have shown regional and seasonal variations in both the incidence and prevalence of PCP, with decreased incidence in eastern and southwestern Europe and a prevalence of PCP in patients with AIDS as low as 5.5%.

As of 2003, a total of 11,587 cases of HIV were reported at a city of 500,000 in central Russia. Assuming 15% of these patients have AIDS, the at-risk population for PCP is 1,738. We estimate that, based on the number of patients in this city with AIDS, and the above ranges for incidence and prevalence of PCP, between 88 and 707 patients could currently have PCP with up to an additional 353 patients developing PCP within the next year.

Conclusion: Despite studies of HIV in Eastern Europe which suggest a low incidence and prevalence of PCP compared with the US/Western Europe, Russia remains at risk for a large patient load with PCP. Bactrim PCP prophylaxis is an effective and low cost means to reducing the incidence of PCP in at-risk patients. It should be routinely prescribed for all HIV+ patients with CD4 <200 cells/mm³.

Do the Cockcroft-Gault and MDRD Equations Give Similar Estimates of Kidney Function in an Ambulatory Elderly Population? M. Bogaisky¹, S. Josyula², J. Winston², M. Swidler^{1,2}, and C. Wyatt^{2,1}Geriatrics and ²Medicine, Mount Sinai Medical School, New York, NY.

Background: Expert guidelines recommend use of either the Cockcroft-Gault (CG) or the MDRD equation for the estimation of kidney function in adults. However, neither equation has been well-validated in elderly adults. It has also not been shown that the two provide similar estimates of kidney function in an ambulatory elderly population.

Objective: To determine if the CG and the MDRD equations yield clinically significant differences in estimates of kidney function in an ambulatory elderly population.

Methods: Data from all patients over the age of 65 seen in a geriatric clinic from August 1, 2004 to August 1, 2005 were abstracted. The most recent outpatient creatinine was chosen. To exclude patients with acute renal failure, those with a creatinine greater than 0.2 mg/dL above their recent baseline values or with only one recorded creatinine were excluded. The standard version of the CG equation and the simplified version of the MDRD equation were used. For the CG equation, the closest weight within one month of the creatinine assay was used and results were not adjusted for body surface area.

Results: A total of 1,264 of 1,990 subjects met criteria to compute both an MDRD and CG estimate of GFR. The average age was 81.4 (SD:

7.6), 80% were female, 40% white, 27% black and 31% Hispanic. When stratified by stage of chronic kidney disease (GFR<15, 15–29, 30–59, 60–89 and ≥90) 61% of subjects were staged differently by the two equations. In 92% of these cases the CG placed subjects in a worse stage than the MDRD. The average difference in GFR between the CG and MDRD estimates in these cases was 26.2 mL/min (SD: 19.5). In 116 subjects (9.2% of the population) the CG GFR was <30 while the MDRD was >30 (mean difference=22.8 mL/min, SD: 11.6). The CG equation found 60% of subjects with a GFR <60 while the MDRD gave only 25% of subjects a GFR <60.

Conclusions: The Cockcroft-Gault and MDRD equations yield clinically significant differences in estimates of kidney function when applied to an elderly ambulatory clinic population. The Cockcroft-Gault equation was more conservative. Validation of these equations in the elderly against a gold standard measurement is necessary.

Nuclear Import of Dendrin, a Novel Glomerular Slit Diaphragm Protein. K. Campbell and P. Mundel. Department of Medicine, Division of Nephrology, Mount Sinai School of Medicine, New York, NY.

Kidney podocytes and their slit diaphragms form the final barrier to urinary protein loss. There is mounting evidence that slit diaphragm proteins may participate in signaling pathways.

Dendrin, a protein originally identified in telencephalic dendrites, is a novel constituent of the slit diaphragm signaling complex where it binds to nephrin and CD2AP. In experimental crescentic glomerulonephritis, dendrin relocates from the slit diaphragm to the nucleus of injured podocytes. Functionally, in heterologous cells, dendrin increases AP1 signaling. The AP1 signaling requires the nuclear import of dendrin because it is significantly impaired in cells transfected with a dendrin construct lacking a functional nuclear localization signal.

Nuclear accumulation of dendrin is abrogated in podocytes cultured in serum-starved medium containing 0.2% fetal bovine serum. Furthermore, exposure of serum-starved cultured podocytes transforming growth factor-beta (TGF-β) at a dose sufficient to induce apoptosis (5 ng/mL) stimulated nuclear accumulation of dendrin noted as early as 30 minutes.

Nuclear expression of dendrin is associated with enhanced TGF-β and staurosporine-induced apoptosis in HEK 293 cells as determined by an Annexin-V based apoptosis assay.

These results suggest a novel signaling pathway whereby dendrin is shuttled from the glomerular slit diaphragm to the podocyte nucleus in the setting of TGF-β mediated apoptosis where it exerts pro-apoptotic effects by increasing the expression of as yet unidentified genetic targets.

Validation Study of a Semi-automated Program for Quantification of Atherosclerotic Burden by Magnetic Resonance Imaging. B.G. Choi¹, C.A. Novoselsky², G. Vilahur¹, D. Yadegar³, and J.J. Badimon¹; ¹The Mount Sinai Hospital, New York, NY; ²Cabrini Medical Center, New York, NY; and ³Lenox Hill Hospital, New York, NY.

Introduction: Practical implementation of magnetic resonance imaging (MRI) for the noninvasive screening of atherosclerosis is limited by inter- and intra-observer variability and labor intensity of morphometric analysis by manual planimetry (MANU).

Hypothesis: We assessed the hypothesis that a semi-automated quantification program (AUTO) for MRI would be faster and more accurate than MANU without loss of reliability.

Methods: Transverse images of the carotid arteries of asymptomatic hyperlipidemic patients (n=17) were obtained by 1.5T whole-body MRI with a 4-element phased-array coil. AUTO, programmed on ImageJ (NIH; Bethesda, MD), segments the images by change in signal intensity from lumen center to vessel outer wall in a serial circular array: lumen area (LA) is lumen center to lumen wall; vessel wall area (VWA) is lumen wall to vessel outer wall; vessel wall thickness is linear distance from lumen wall to vessel outer wall. Automated image post-processing with observer supervision identifies and corrects outlier segments. Images were each processed twice by two independent observers who repeated the same analysis by MANU. *In vivo* imaging of rabbits with atherosclerotic aortas (n=3) was similarly obtained and then sacrificed to confirm histopathologic correlation.

Results: Analysis time per image (seconds±SD) was 17.4±3.1 (AUTO) versus 87.3±19.4 (MANU), p<0.001. Inter- and intra-observer differences for carotid measurements were not significant for both AUTO and MANU (see Table); however, there was stronger correlation between animal histopathology and AUTO (r=0.87, p<0.0001) than with MANU (r=0.74, p<0.0001). Bland-Altman analysis did not demonstrate any systematic bias.

Conclusion: AUTO is superior to MANU in speed and histopathologic correlation without significant differences in inter- and intra-observer variability. Implementation of AUTO may facilitate MRI for the screening of the burden of atherosclerotic disease.

TABLE
Mean Inter- and Intra-observer Differences between Observations

		Lumen Area (%)	Vessel Wall Area (%)	Vessel Wall Thickness (%)
M	Interobserver	6.6	4.6	5.3
A		(p=0.32)	(p=0.27)	(p=0.09)
N	Intraobserver	2.8	3.0	2.3
U		(p=0.68)	(p=0.47)	(p=0.47)
A	Interobserver	3.9	4.0	4.2
U		(p=0.50)	(p=0.45)	(p=0.61)
T	Intraobserver	0.7	2.1	0.2
O		(p=0.91)	(p=0.70)	(p=0.96)

Platelet Function in Clopidogrel-Treated Subjects is Recoverable by Addition of Donated Platelets: Implications for Urgent Surgical Management in Acute Coronary Syndrome. B.G. Choi^{1,2}, G. Vilahur¹, M.U. Zafar^{1,2}, J.F. Viles-Gonzalez¹, V. Fuster², and J.J. Badimon^{1,2}. ¹Cardiovascular Biology Research Laboratory and ²Zena and Michael A. Wiener Cardiovascular Institute, Mount Sinai School of Medicine, New York, NY.

Background: Aspirin (ASA) and clopidogrel are commonly used in the treatment of acute coronary syndrome, but their long anti-platelet effect may delay surgery if required. We studied the possibility of normalizing platelet reactivity after clopidogrel + ASA treatment.

Methods: We performed a randomized cross-over study of healthy subjects (n=11, age 35 ± 5 years) receiving a loading dose of either 300-mg or 600-mg clopidogrel + 325 mg ASA, followed by 75 mg clopidogrel + 81 mg ASA daily for 2 days. Platelet reactivity was assessed by light transmittance aggregometry (LTA) and flow cytometry pre-treatment, 4h- and 72h- post-load. To normalize platelet reactivity, increasing amounts of pooled platelets (20%, 40%, 50%, and 60% of total platelet rich plasma [PRP] volume) from 5 untreated volunteers (pooled V-PRP) were added *ex vivo* to the subjects treated PRP (S-PRP). Adenosine diphosphate (ADP) (10 μM), arachidonic acid (AA) (1 mM), collagen (2 and 5 μg/mL), and TRAP (10 μM) served as agonists. By flow cytometry, we assessed activation by GPIIb/IIIa receptor exposure in the ADP-stimulated platelets.

Results: At both 4- and 72-h post-treatment, addition of 50% (300 mg arm) and 60% (600 mg arm) of V-PRP normalized ADP-induced platelet aggregation. Recovery of function was linear with each incremental increase of V-PRP. Addition of 20% V-PRP normalized platelet reactivity when challenged by TRAP whereas 40% V-PRP was required to normalize platelet function to AA and collagen at both 4- and 72-h. A minimum of 40% or 50% V-PRP were needed to overcome platelet disaggregation in the 300 mg or 600 mg arms, respectively. ADP-induced GPIIb/IIIa activation showed the same pattern as LTA (r=0.74).

Conclusions: Pre-operative transfusion of 10 platelet units (the equivalent of 40% V-PRP, see Table) after 300 mg clopidogrel loading or 15 units after 600 mg loading may reverse clopidogrel-induced platelet disaggregation. These doses *ex vivo* also fully normalized the response to AA and collagen. Pre-operative prophylactic transfusion may allow patients to benefit from clopidogrel's anti-platelet effect to the time of transfusion, shorten hospitalization, and decrease post-operative bleeding. Our findings deserve to be fully explored in a clinical trial.

TABLE
Dose Conversion Table for V-PRP to Platelet Units

% Added Pooled V-PRP	Platelet Units	Platelet Pools
20%	7.5	1–2
40%	10	2
50%	15	3
60%	22.5	4–5

Assumptions: One platelet pool increases platelet count by 10,000/μL, 5 platelet units = 1 platelet pool, mean platelet count 150 × 10⁶.

Selective Estrogen Receptor Modulation Reduces Characteristics of Plaque Vulnerability. B.G. Choi^{1,2}, G. Vlahuri¹, M.U. Zafar^{1,2}, L. Cardoso³, D. Yadegar¹, J.F. Viles-Gonzalez¹, M.B. Schaffler³, V. Fuster², and J.J. Badimon^{1,2}. Cardiovascular Biology Research Laboratory¹, Zena and Michael A. Wiener Cardiovascular Institute², Leni and Peter W. May Department of Orthopaedics³, Mount Sinai School of Medicine, New York, NY.

Objectives: We assessed the hypothesis that selective estrogen receptor modulation with raloxifene induces changes in atherosclerotic lesions to a more stable plaque phenotype.

Background: Estrogen therapy (ET) is associated with increased cardiovascular events in post-menopausal women, but post-hoc analysis from an osteoporosis treatment trial (the Multiple Outcomes of Raloxifene Evaluation, MORE) conducted in the 1990s suggests that raloxifene decreased cardiovascular events in high-risk women, i.e., those most likely to have preexisting atherosclerotic lesions. The modern Raloxifene Use for the Heart (RUTH) study seeks to confirm whether this benefit is sustained on top of optimal pharmacologic therapy for coronary artery disease, but a mechanism of action for raloxifene's putative cardiovascular benefit is unclear. Some studies suggest an anti-inflammatory effect unlike ET; furthermore, *in vitro* studies point to possible changes in the morphology of vascular calcification with raloxifene that may have implications upon plaque stability.

Methods: Atherosclerosis was induced in 42 ovariectomized New Zealand White rabbits. The animals were then imaged by magnetic resonance (MRI) for baseline atherosclerosis measurement and randomized to control (OVX, n=12), raloxifene therapy (RLX, n=24), or immediate sacrifice (n=6) for immunohistopathologic correlation of MRI observations. Six months after randomization, rabbits underwent repeat MRI and then sacrifice for *ex vivo* micro-computed tomography (μ CT) and molecular analysis.

Results: Unlike OVX, RLX significantly reduced the atheroma volume of previously established lesions ($-5.5 \pm 4.5\%$, $p<0.05$) as assessed by MRI; histopathologic analysis indicated volume reduction from 35% less lipid deposition ($p<0.05$) and 37% less macrophage content ($p<0.05$). Analysis for lesion inflammation revealed significant reductions (all $p<0.05$) in cyclooxygenase-2 (COX-2) by 60%, matrix metalloproteinase-1 by 50%, and monocyte chemoattractant protein-1 expression by 27% in RLX vs. OVX. μ CT showed similar total vascular calcification between groups, but calcifications in RLX were less nodular and had better radial organization (mean calcific arc angle $63 \pm 7^\circ$ vs. $33 \pm 6^\circ$ in OVX, $p<0.01$), the predicted result of a 53% increase in bone morphogenetic protein-2 expression ($p<0.05$). The changes in plaque activity appear to be mediated through raloxifene's effect on estrogen receptor α which doubled in expression in RLX ($p<0.001$). Notably despite COX-2 inhibition, arterial whole-blood platelet aggregation in decreased when challenged by adenosine diphosphate ($p<0.01$).

Conclusions: Treatment with raloxifene results in regression of established atherosclerotic lesions, enhanced formation of calcification in a pattern associated with plaque stability, and decreased inflammation. Collectively these observations suggest that raloxifene may not have a deleterious effect on plaque stability.

Adjusting CPK Measurements for LV Mass to Determine Infarct Severity. S. Choudry, G. Lanier, L.B. Croft, and M.E. Goldman. Mount Sinai School of Medicine, New York, NY.

Background: Serum creatinine phosphokinase (CPK) levels have been shown to correlate with the mass of cardiac tissue that is damaged during a myocardial infarction (MI), and infarct size in turn has been correlated with prognosis. However, quantification of infarct size based solely on serum CPK levels, while supplying information about the mass of infarcted tissue, does not account for a patient's total ventricular mass. This method, therefore, may misrepresent the severity of an infarct in those patients with smaller or larger left ventricular (LV) mass. Adjustment of CPK levels for LV mass may provide a more accurate assessment of infarct severity, and therefore prognosis, in a given patient.

Methods: A retrospective cohort analysis was performed. Patients were selected for inclusion in the study from a review of all consecutive admissions to the Coronary Care Unit at Mount Sinai Hospital from July 2004 until December 2005. Patients with renal insufficiency, symptoms of chest pain lasting more than 24 hours, documented previous MI, or known prior LV dysfunction were excluded from the study. Patient demographic information, cardiac catheterization data, and echocardiographic parameters (when available), were recorded. The collected data was then analyzed for significant relationships between enzymatic measures of infarct size, LV mass, and degree of LV dysfunction.

Results: Sixty-two patients met the inclusion criteria for our study. No significant relationship between enzymatic measures of infarct size and degree of LV dysfunction was found. However, we found a significant

relationship between left ventricular mass, as measured by echo, and body surface area (BSA) ($r=0.6046$, $p=0.007$). It is also notable that patients with a larger BSA had a significantly larger CPK than those with a smaller BSA (mean CPK 1001 vs. 605, $p=0.047$). In the subgroup of patients with a large MI, the patient's BSA significantly correlated with CPK at the time of catheterization ($r=0.4172$, $p=0.04$).

Conclusion: No significant relationship could be seen between enzymatic measures of infarct size and LV dysfunction when adjusted for left ventricular mass. This may be due to the small size of our study. Interestingly, patients with a larger BSA were found to have significantly higher enzymatic markers of MI. This suggests that an MI may be more difficult to detect in those patients with a smaller BSA, a finding that would need to be confirmed in larger studies.

Realistic Expectations about Publication Following a Year of Clinical Research. B. Cohen, E. Friedman, and K. Zier. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

Purpose of Study: Many medical students who undertake a one year research fellowship expect that their work will result in a publication. Moreover, residency directors may hold the same expectation. The objective of this study was to document the publication rates of participants in one year research programs to provide a reasonable standard against which to judge productivity.

Methodology: Names of students and their mentors who participated in the NIH Clinical Research Training Program (CRTP) and the Doris Duke Clinical Research Fellowship from 2001–2004 were provided by the programs. Publications resulting from the fellowship year were tracked up to 18 months post-fellowship using PubMed.

Summary of Results: From 7/2001 to 6/2004, of 217 fellows, 24% had at least 1 publication 6 months post-fellowship. Publication rates increased with time, with 50% publishing 18 months after program completion. 69% of fellows who published had at least one first author publication. 55% of the publications generated by 6 months were original research, 34% were review articles, and 11% were case reports.

Conclusions: The results demonstrate that although about half of the participants in these programs are able to publish within 18 months of completion of their fellowship, since most participants complete their fellowships after their third year of school, only a minority will have published by the time they apply for residency. This information should provide Deans (Student Affairs, Research), students, and program directors with more realistic expectations for the outcomes of this medical school research experience.

SPECT Myocardial Perfusion Imaging in Morbidly Obese Patients: Image Quality, Hemodynamic Response to Pharmacologic Stress, and Diagnostic and Prognostic Value. W.L. Duvall, L.B. Croft, J.S. Corriel, A.J. Einstein, J.E. Fisher, P.S. Haynes, R.K. Rose, and M.J. Henzlova. Mount Sinai School of Medicine, New York, NY.

Background: Obesity is a growing epidemic in the United States, and little is known about the characteristics of the morbidly obese population (body mass index [BMI] >40 kg/m²) undergoing stress myocardial perfusion imaging (MPI).

Methods and Results: We retrospectively reviewed all consecutive morbidly obese patients without known coronary artery disease presenting for a clinically indicated technetium 99m gated stress single photon emission computed tomography imaging study over a 42-month period. Studies were analyzed for image quality, for the contribution of attenuation correction to image interpretation, and for the hemodynamic response to pharmacologic stress. In patients who subsequently had cardiac catheterization, the results were compared with those from the initial MPI study, and the Social Security Death Index and hospital medical records were searched to the assess survival rate in the entire cohort. A total of 433 patients were identified with a mean BMI of 47.3 ± 8 kg/m² and a mean Tc-99m stress dose of 35.6 ± 5.4 mCi. Image quality was good in 61% of the patients, adequate in 37%, and poor in 2%. It was found to be dependent on the stressor used (better with exercise) but did not correlate with increasing weight or BMI. Attenuation correction was used in 95% of the studies reviewed and was helpful for image interpretation in 60%. The heart rate response to dipyridamole and adenosine was more pronounced and the blood pressure response to dipyridamole was less pronounced in morbidly obese patients compared with nonobese control patients. In the 43 patients who underwent catheterization, stress MPI had a sensitivity of 95% and negative predictive value of 80%. Kaplan-Meier survival analysis at 1 year showed a significant difference in survival rate of 98.3% for normal MPI studies and 94.0% for abnormal MPI studies ($p = 0.02$).

Conclusion: Diagnostic-quality single photon emission computed tomography imaging is feasible in the majority (98%) of morbidly obese patients with the use of a dual-head camera, attenuation correction, and high stress Tc-99m tracer doses. Exercise stress was associated with better image quality. The prognostic value of a normal MPI study in this population appears to be less favorable than in non-morbidly obese patients (J Nucl Cardiol 2006; 13:202–209).

AL Amyloid and Rheumatic Disease: Cause and Consequence. J.T. Diep, H. Blumstein, A. Solomon, D. Weiss, C.L. Murphy, Q. Guo, and P.D. Gorevic. Departments of Medicine, University of Tennessee at Knoxville, and Mount Sinai School of Medicine. New York, NY.

Background: Although secondary (AA) amyloidosis is well recognized as an uncommon complication of rheumatoid arthritis or spondyloarthritis, relationships between amyloid due to immunoglobulin light chain deposition (AL) and rheumatic disease have been less appreciated. AL may be organ-dominant, or may involve multiple organ systems; it may simulate Sjogren's syndrome (SS), rheumatoid arthritis, polymyalgia rheumatica/giant cell arteritis, and rarely scleroderma.

Methods: AL subunit proteins were characterized from either formalin-fixed or frozen tissue by microsequencing. V-region gene amplification and sequence analysis was used for the identification of specific precursor light chain production in bone marrow, and to correlate with germ-line, rearranged $\lambda 3r$ genes in the normal PBMC repertoire, and those mutated / significantly overrepresented in AL amyloid.

Results: We reviewed five patients with AL amyloidosis and rheumatic disease; four with a Sjogren's-like syndrome and one presenting as a scleroderma-like illness. Type of amyloid was established by immunohistology, or by microsequencing. Localized AL in SS presented as cutaneous nodules (1), a waxy macular lesion (1), or multiple pulmonary nodules (amyloidomas), with no evidence of systemic deposits; in one patient however, pinch purpura biopsied as AL, leading to the recognition of gammopathy, visceral amyloid, and plasma cell dyscrasia. The fifth patient presented with a scleroderma-like illness, consisting of tightening skin, decreased oral aperture, dysphagia and myalgias. Recognition of atypical features led to a deep skin and muscle biopsy that showed amyloidosis; further work-up revealed monoclonal λ light chains in serum and urine, lytic lesions typical of multiple myeloma, and 40% plasma cells in bone marrow. Microsequence analysis of Bence-Jones protein (BJP) and amyloid peptides extracted from the formalin-fixed skin biopsy yielded residues 3-21 (FR1) and 40-53 (FR2) of a $\lambda 3r$ light chain, the germ-line sequence of which was used to amplify and sequence the entire V-region gene by amplification from a single slide of unfixed bone marrow.

Conclusion: The association between AL and Sjogren's- or scleroderma-like diseases is reviewed, and may be the result of systemic disease leading to the diagnosis of myeloma, or organ-specific amyloid in which localization may reflect structural features of specific light chains and/or an antigen-driven pathogenic mechanism.

The Regulation of the Maxi-K Channel in the Distal Nephron. G. Estilo. Mount Sinai School of Medicine, New York, NY.

Within the kidney, the connecting tubule (CNT) and the cortical collecting duct (CCD) are primarily responsible for K secretion. Two apical K-selective channels have been functionally identified in the CNT and CCD: the secretory K (SK) and the maxi-K (BK) channel. Whereas the SK channel mediates baseline K secretion, the maxi-K channel is considered to be involved in flow-stimulated K secretion. The renal response to dietary K loading includes an increase in urinary K excretion, due in large part to enhanced K secretion in the distal nephron. Recent data from our group has demonstrated a role for the maxi-K channel in renal K adaptation. Dietary K loading led to an increase in abundance of maxi-K mRNA transcripts, enhanced flow-stimulated net K secretion in microperfused CCDs, and a redistribution of immunodetectable channel proteins from an intracellular pool to the apical membrane. This adaptation could be mediated by a tran-

sient increase in plasma K concentration but could also be initiated by a dietary K-induced increase in circulating levels of aldosterone. To test our hypothesis that aldosterone regulates maxi-K channel expression and activity in the CCD, New Zealand white rabbits were fed low Na and high Na diets, the former to increase circulating levels of aldosterone, for 10 days. At time of sacrifice, serum and urine were collected for measurement of Na, K, and aldosterone concentrations, results of which are depicted in the **Table** below. As expected, rabbits fed the low Na diet excreted no urinary Na and had higher circulating levels of aldosterone than the rabbits fed the high Na diet. There were no significant differences between serum [Na] and [K] in the two experimental groups. Real-time PCR quantitation of mRNA encoding maxi-K α - and β - subunits in isolated CCDs from high Na and low Na-fed rabbits are being analyzed. Indirect immunofluorescence microscopy will also be utilized to study the effects of aldosterone on localization of channel proteins. Preliminary data from a single transport study of a CCD isolated from a low Na-fed rabbit demonstrated an increase in net K secretion and Na absorption as tubular flow rate was increased from slow physiologic ($\sim 1 \text{ nL}\cdot\text{min}^{-1}\cdot\text{mm}^{-1}$) to fast ($\sim 5 \text{ nL}\cdot\text{min}^{-1}\cdot\text{mm}^{-1}$). This data suggests that aldosterone, in the setting of normokalemia, stimulates maxi-K channel expression activity in the distal nephron.

How Much Time Do Geriatricians Spend in Nonreimbursable Care Coordination? J. Farber. Mount Sinai School of Medicine, New York, NY.

Background: Geriatrics practice involves nonreimbursed care coordination interactions with patients, caregivers and others outside the office visit. The purpose of this study is to describe the amount and nature of time geriatricians spend providing nonreimbursable care coordination.

Methods: Physicians in a large academic geriatric ambulatory practice with at least two half-days of office visits scheduled in the week were selected to participate. Participants were briefed and provided a written protocol, along with structured interaction forms to document all clinical interactions outside of office visits during one of three randomly selected one-week periods from November 2005 through January 2006. Physicians were encouraged to complete the interaction forms at the time the work was performed to minimize uncaptured events and to document time spent to the nearest minute. Information about the participant in the interaction, and the mode, nature and outcome of the interaction were collected. Time spent is reported in three ways: (1) mean time involved in these interactions, (2) mean time spent relative to the physician's time spent seeing patients that week, and (3) mean time spent relative to the number of patients on the physician's panel. Linked interactions were grouped into episodes of care.

Results: Data were obtained from 9 fellows and 7 attendings for a total of 27 physician-weeks, representing 68% of ambulatory sessions for eligible physicians. Data consisted of 475 discrete interactions representing 300 episodes of care involving 231 patients. Mean interaction duration was 6.38 minutes (S.D. 7.36, range 0.5–120). Interactions were significantly longer when they involved the patient or family vs. all others (7.31 vs. 5.52 mins, $p=0.008$), and when temporally unrelated to an office visit (6.92 vs. 5.30 mins, $p=0.02$). There were no significant differences between fellows and attendings (6.43 vs. 6.27 mins, $p=0.82$), interactions involving patients with and without dementia (6.98 vs. 5.88 mins, $p=0.11$), and with physician's own patients vs. coverage (6.60 vs. 4.60 mins, $p=0.06$). Physicians spent, on average, an additional 18.7 minutes performing care coordination per 30 minutes of seeing patients in the office. Physicians spent 1.85 minutes performing care coordination per patient on the physician's panel per week. Episodes involving care coordination or counseling were statistically significantly longer in duration than those involving acute issues (22.8 vs. 12.8 mins, $p<0.05$). 36% of episodes involving acute issues resulted in medication use, 27% in an office visit, and 9% in a referral to another physician. 33% of interactions occurred within 1 week of an office visit. Of these, 58% followed the office visit, 34% preceded the visit, and 8% occurred on the same day. 78% of interactions were telephonic, 8% electronic, and 8% face-to-face. 24% of interactions took place with the patient, 24% with the family, 12% with another MD or NP, and 12% with a visiting nurse.

TABLE
Effect of "Low" and "High" Na Diet on Serum and Urine Electrolytes

Serum aldosterone (ng/dL)	n	Serum Na, mEq/L	Serum K, mEq/L	Urine Na, mEq/L	Urine K, mEq/L
Low Na	5	133.8 \pm 1.6	4.7 \pm 0.2	0*	243.7 \pm 50.4
High Na	3	141.8 \pm 2.3	4.7 \pm 0.4	78.6 \pm 3.8	263.3 \pm 50.6
					75.6 \pm 21.8
					8.9

All results are expressed as means \pm SE. n refers to the number of animals studied. * $p<0.05$ compared to "High Na."

Conclusions: Geriatricians spent 18.7 minutes in nonreimbursable clinical interactions for every 30 minutes of seeing patients in the office. For a full-time geriatrician (16 visits/day over 5 days/week) this translates into an extra 25.0 hours of nonreimbursable clinical work/week. At least two-thirds of the interactions in this study were not temporally associated with a billable office visit. Episodes involving care coordination and counseling may span several interactions totaling over 20 minutes.

Barriers to Caring for Chronic Hepatitis C in HIV (“Co-infected”) Patients. B. Forsyth and D. Fishbein. Mount Sinai School of Medicine, New York, NY.

Background: Chronic hepatitis C virus (HCV) is highly prevalent in HIV patients. Although end-stage liver disease (ESLD) is the leading cause of morbidity and mortality in hospitalized HIV patients, the majority of co-infected patients are not receiving HCV treatment. In this study we examine *provider* barriers to HCV treatment in HIV.

Methods: Anonymous surveys were distributed to all health care providers attending the International AIDS Society meeting in NYC in October 2005. The surveys contained knowledge, attitude and practice questions regarding co-infection.

Results: Of the 505 received surveys 244 (48%) were completed. The respondents were primarily nurse practitioners (NP) or physician assistants (PA) (29%), and physicians (55%); mean age was 45.3 ±10 with a median practice experience of 14 years. Half the providers self-reported referring <25% of their patients for HCV treatment. And 52% of providers report NOT referring for HCV treatment as often as they think they should, while 42% report NOT initiating HCV treatment as often as they think they should. Both groups cite “Patient does not want treatment” among their top three reasons. Physicians were significantly less likely than NPs/PAs to refer for this reason (OR 0.23; CI 0.09–0.59), however there was no difference between these groups in initiating treatment. Of those who DID refer and initiate as often as they thought they should, “we have an easy referral process” and “the risk of ESLD outweighs the risk of not treating,” were among the most cited reasons. Many providers are not treating HCV themselves (69%), but would be willing if they had appropriate training (58%) and time and resources (66%).

Conclusions: Many HIV providers report discomfort in treating HCV without a referral. However, with additional training, resources and time they would likely increase their treatment rates. A significant barrier to the provision of HCV treatment is provider perception that patients themselves do not want treatment. Further exploration of this barrier is recommended to increase the percentage HIV patients receiving HCV care.

Dyspnea and Chylous Pleural Effusion in a 50-Year-Old Female. J. Freedman. Mount Sinai School of Medicine, New York, NY.

A 50-year-old woman was admitted to the hospital with dyspnea and a large right-sided pleural effusion which proved to be chylous. Further investigations led to a diagnosis of pulmonary lymphangioliomyomatosis (LAM), a rare debilitating disease usually seen in women of childbearing age. Pulmonary LAM is characterized by peribronchial, perivascular, and perilymphatic non-neoplastic proliferation of smooth muscle cells. These changes are associated with recurrent spontaneous pneumothorax, pulmonary hemorrhage, chylous effusions, bronchial cyst formation, and progressive loss of lung function. In addition, there is an absence of associated inflammation or organized fibrosis with the predominant finding being numerous thin-walled cysts throughout both lungs. This patient’s case is unusual in that she was post-menopausal upon presentation with a relatively short duration of symptoms prior to diagnosis. The case is presented in full, followed by a review of the available literature on pulmonary LAM focusing on differential diagnosis, radiologic and pathologic findings, clinical course, and management.

Translational Regulation of Gene Expression of NPM-ALK Kinase of Anaplastic Large Cell Lymphoma. K. Funato, N. Haq, Y. Sun, J. Chen, G. Khitrov, W. Zhang and D.W. Sternberg. Division of Hematology and Oncology, Mount Sinai School of Medicine. New York, NY.

NPM-ALK is an activated tyrosine kinase generated by the t(2;5)(p23;q35) chromosomal translocation associated with 50% of anaplastic large-cell lymphoma. Nucleophosmin-anaplastic lymphoma kinase (NPM-ALK) is known to play a causal role in the generation of hematopoietic neoplasia, and it has a multiple tyrosine residues that can bind to signaling proteins. We have found that expression of NPM-ALK

regulates mediators of translational initiation, such as mTOR, S6K1, and 4E-BP1. These findings stimulated our hypothesis that NPM-ALK promotes neoplasia by altering the partitioning of specific mRNAs to polysomes and hence regulates the translation of specific mRNA molecules. In this study, we generated Ba/F3 murine hematopoietic cells transduced with a kinase-active NPM-ALK or a kinase-deficient NPM-ALK mutant (K210A). Our goal was the determination of the global profile of polysome-associated mRNA regulated by NPM-ALK kinase activity. We purified polysomal and total RNA from cell lysates, and we assessed the global profile of gene expression using Affymetrix mouse genome microarrays. Although we found little difference in total mRNA levels, we identified 286 genes altered significantly in the polysomal mRNA fractions. These included several of immediate interest to the pathogenesis of hematopoietic neoplasia. For example, Lyl1 or Tal1 are genes both associated with poor prognosis in T-cell acute lymphoblastic leukemia, and each of the respective mRNA’s was enriched in the polysomal RNA fraction of cells with kinase active NPM-ALK. Our findings demonstrate the feasibility of assessing NPM-ALK-regulated gene expression through translational initiation, and these results suggest that polysome partitioning of mRNA species might be a locus of gene regulation in NPM-ALK-derived neoplasia.

Macrophage Phagocytosis of Apoptotic Cholangiocytes *in vivo* Is Impaired in PBC. J. Garber. Mount Sinai School of Medicine, New York, NY.

Introduction: Animal models suggest impaired macrophage phagocytosis of potentially immunogenic apoptotic cells plays a role in autoimmune disease. The consequent increased phagocytosis of apoptotic cells by dendritic cells can be pro-immunogenic under inflammatory conditions. Most primary biliary cirrhosis (PBC) patients have a quantitative decrease in phagocytosis of apoptotic cells by cultured monocyte-derived macrophages.

Aims: (1) To examine macrophage expression and function of CD14 and complement receptor 3 (CR3), receptors known to be involved in internalization of bound apoptotic cells. (2) Identify the cell types involved in apoptotic cholangiocyte phagocytosis *in vivo* in normal controls and patients with PBC, primary sclerosing cholangitis (PSC), and mild acute rejection post-liver transplantation.

Patients and Methods: Blood was collected from 5 AMA+ PBC patients (stage 1–2) and 5 healthy controls, matched for age and gender. Isolated monocytes were cultured for 5 days in serum-free medium or medium plus 10% fetal calf serum. On day 5, the monocyte-derived macrophages were co-cultured with apoptotic human salivary gland epithelial cells previously stained with carboxy-fluorescein succinyl ester (CFSE). After 2 hours, non-adherent cells were removed, pelleted, and the supernatant was collected. Adherent cells were stained with mAbs against CD14 and CD11b (CR3) and subjected to flow cytometry. For immunohistochemistry, liver sections prepared from paraffin-embedded, formalin-fixed early stage biopsy specimens (5 for each diagnosis) were stained with mAb against either CD68 (expressed by macrophages and dendritic cells), CD163 (macrophages only), or CD83 (activated dendritic cells only) and counterstained with hematoxylin.

Results: Phagocytosis of apoptotic cells was significantly impaired by 35–70% in each PBC patient relative to controls. In normal controls, CD11b and CD14 expression were unaffected by phagocytosis of apoptotic cells. In the PBC patients, CD11b, not CD14, surface expression decreased significantly (>50%) following phagocytosis of apoptotic cells in both the presence and absence of serum. Immunohistochemical staining revealed CD68+, CD163-, CD83+ cells (dendritic cells) crossing the basement membrane and surrounding 80–90% of apoptotic cholangiocytes in the PBC biopsies. Apoptotic bodies were also observed within the cytosol of cholangiocytes and detached from the basement membrane. In the mild rejection biopsies, CD68+, CD163+, CD83- cells (macrophages) were most frequently observed surrounding the apoptotic cholangiocytes (70–85%). Too few apoptotic cholangiocytes were observed in the PSC and normal biopsies for analysis.

Conclusion: Macrophage phagocytosis of apoptotic cholangiocytes *in vivo* is decreased in PBC compared to mild rejection and may be due to CR3 dysfunction.

Indefinite Anticoagulation for Pulmonary Embolism in the Elderly: Benefits and Risks Forecasted by Decision-Tree Analysis and Markov Modeling. J. Haspel. Mount Sinai School of Medicine, New York, NY.

Treatment of venous thromboembolism (VTE) in the elderly represents a unique situation where the benefits and risks of anticoagulation are difficult to balance. This is particularly true with respect to pulmonary

embolism (PE), which has a heightened recurrence rate and is more likely to re-present fatally. However, elderly individuals are also more likely to suffer bleeding complications and are at increased risk for falls that can lead to intra-cranial hemorrhage (ICH). To better understand the risks and benefits of treating idiopathic PE in elderly, fall-prone patients, this project utilized decision analysis to compare indefinite anticoagulation with coumadin to finite anticoagulation in the treatment of this disorder. Both Decision-Tree and Markov simulation methodologies were employed to forecast clinical outcomes, such as total survival, event-free survival, QALY score and death, out to 5 years. The results suggest a favorable profile for indefinite anticoagulation with an ARR of $3.5\% \pm 0.15$ for total survival, $20\% \pm 1.1$ for event-free survival, and an average gain of 146 ± 18 QALY-days by 5 years. The benefits of continued coumadin use increased progressively with time. Both Decision Tree analysis and Markov modeling produced similar results. Sensitivity analysis suggested that the ARR for total survival was sensitive to variations in several rates, including PE recurrence rate off coumadin (point of equivalence ~3%), GIB rate on coumadin (point of equivalence ~10%), and yearly all-cause mortality (point of equivalence ~10–20%). However, event-free survival more robustly favored long-term coumadin, even with PE recurrence rates as low as 1%, yearly all-cause mortality as high as 50%, and yearly all-cause hospitalization rate as high as 40%. Taken together, the data suggests that elderly, fall-prone patients who have had an idiopathic PE would benefit from indefinite anticoagulation compared to a finite course of 6–12 months. While elderly, frequently falling patients have a higher bleeding risk than younger patients, this is outweighed by the reduction in the rate of recurrent VTE and its complications. However, for sub-groups of patients who are known to have significantly lower PE recurrence rates (such as women or patients with total thrombus resolution) or patients with significantly heightened bleeding risks (such as cirrhotic patients), finite courses of coumadin may produce an equivalent benefit to long-term therapy.

BTNL-2 Gene Variation—A Potential Association with Sarcoidosis. J. Hsieh. Mount Sinai School of Medicine, New York, NY.

Sarcoidosis is a multiorgan granulomatous inflammatory disease of exaggerated cellular immune response. Although the exact pathogenesis of sarcoidosis remains unclear, familial aggregation studies have demonstrated a significant genetic component. Previously identified by single nucleotide polymorphism (SNP) scan, a single SNP (rs2076530; G/A) in the butrophilin-like 2 (BTNL-2) gene has been strongly associated with sarcoidosis in a white German population and to a lesser extent in African Americans. BTNL-2 is a member of the immunoglobulin gene family and is related to the B7 co-stimulatory receptor, although its exact function is unknown. Optimal T-cell activation involves antigen binding to the T-cell receptor and additional co-stimulatory interactions such as the binding of CD 28 expressed on T-cells to B7 on antigen presenting cells (APCs). rs2076530 introduces a frameshift and premature termination of BTNL-2. We propose that this truncated form of BTNL-2 lacks the transmembrane domain, rendering it incapable of inserting into the plasma membrane of APCs and turning off activated T-cells *in situ*. We are currently investigating BTNL-2 protein expression in APCs derived from both cell culture and from human buffy coat samples. These cells will be cultured with various cytokines of known importance in sarcoidosis and other immune-stimulating agents such as LPS. The time course of induction and relative abundance of various BTNL-2 isoforms will be assessed by RT-PCR, northern, and western blot analysis. We hypothesize that in controls, inflammatory cytokines will increase BTNL-2 cell-surface expression so it may participate in the down-regulation of activated T-cells. In sarcoidosis patients with the BTNL-2 gene variant, we propose that APCs expressing the truncated form of BTNL-2 will be unable to express the receptor on the cell surface and thus will be unable to down-regulate activated T-cells, resulting in the exaggerated T-cell response seen in sarcoidosis.

Case Report of Adult Onset Macromastia and Polymastia. L. Huang. Mount Sinai School of Medicine, New York, NY.

Background: While carcinogenesis of the breast has been extensively studied, the role of benign breast hyperplasia in understanding breast development and differentiation has not been as well described.

Objective: We describe an unusual case of adult onset benign polymastia and macromastia. Our goal was to investigate the pathogenesis of this anomaly by searching for growth factor over/under expression that may be leading to abnormal breast tissue growth.

Methods: In this study, we analyzed the expression of growth factors that have been implicated in breast development including progesterone receptor, ER-alpha, ER-beta, IGF1, IGF1-R, aromatase receptor

(AR), TBG-B, TGF-B receptor, and SMAD by immunohistochemistry in paraffin-embedded sections of our patient's native and ectopic breast tissue. Positive findings were then compared to normal controls. Negative findings were not compared to controls.

Results: We found positive staining for AR, IGF-1, and IGF1-R in the patient's tissue. In addition, we found that expression of these factors in the patient's ectopic breast was greater when compared to controls.

Conclusion: While our results are inconclusive as to the definitive pathogenesis of our patient's condition, further investigation in benign breast hyperplasia may yield information as to treatment modalities for our patient, as well as new insight into breast development and differentiation.

Standardized Uptake Value of Stage 1 Non-small Cell Lung Carcinoma, a Predictor of Prognosis after Surgical Resection? A.S. Teirstein, A.M. Huysman, S. Swanson, D. Krellenstein, J. Machac, and J. Gil. Mount Sinai School of Medicine, New York, NY.

Background: The overall 5-year survival rate for non-small cell lung carcinoma (NSCLC) is only 14%. (Ahuja et al.). Although stage 1 patients have the best prognosis for surgical cure, the post-surgical recurrence rate has been reported as high as 35%. (Naruke et al.) The International Adjuvant Lung Cancer Trial Collaborative Group concluded that cisplatin-based chemotherapy improves survival among patients who have undergone complete resection of NSCLC. (IALT Collaborative Group) The intensity of radio-labeled 18F-fluoro-2-deoxy-glucose (FDG) uptake, a measure of increased glucose metabolism recorded as a standardized uptake value (SUV) on positron-emission tomography (PET) scans, has been correlated with the growth rate and proliferative capacity of NSCLC. (Duhaylongsod et al.) The goal of this study was to determine whether the SUV of a tumor on PET predicts prognosis after surgical resection of stage 1 NSCLC and may identify a subgroup of stage 1 NSCLC patients who would benefit from adjuvant treatment.

Methods: A retrospective review of patients who underwent surgical resection of stage 1 NSCLC and had FDG-PET scanning performed preoperatively was undertaken, at The Mount Sinai Medical Center, NYC. The records of 43 patients ranging in age from 53–90 years, and including 32 stage 1A tumors and 13 stage 1B tumors were analyzed. The SUV and size of the tumors were correlated with postoperative recurrence over a follow-up period of at least two years (range of 7–80 months).

Results: The mean SUV of the nodules was $5.62 \text{ g/mL} \pm 4.62$ ($1-21.64 \text{ g/mL}$). Eleven (24%) of the 45 tumors recurred during follow-up. In this sub-group of patients, the mean SUV was $5.55 \text{ g/mL} \pm 4.68$ ($0-14.4 \text{ g/mL}$). This was not significantly different than that of the 45 tumors that did not recur during the follow-up period. In this sub-group of patients without recurrence, the mean SUV was $5.62 \text{ g/mL} \pm 4.69$ ($0-21.64 \text{ g/mL}$). Amongst tumors that recurred, the mean size was 2.94 cm ($1.0-5 \text{ cm}$). Amongst those that did not recur, the mean size was 2.00 cm ($0-5 \text{ cm}$).

Conclusions: SUV was not indicative of prognosis of surgically resected stage 1 lung cancers in this study population. Recurrence was more common in larger tumors but there was a large overlap in size between recurrence and no recurrence. The small size of stage 1 tumors may inherently limit the utility of SUV as a prognosticator. We propose that currently, indices of prognosis must comprise multiple factors, including SUV, size, cell type, and molecular biology.

Barriers to HIV Testing in a Large, Urban Academic Medical Center. C. Jain¹, J. Shin¹, C. Wyatt¹, F. Wallach¹, R. MacKay¹, and S. Jones². ¹Mount Sinai School of Medicine, New York, NY and ²Cornell University Medical Center, New York, NY.

Background/Objectives: Despite the 1993 CDC recommendation for routine, voluntary HIV testing in communities with an HIV prevalence >1%, up to 40% of patients are still diagnosed with CD4 counts less than 200. Patients have come into contact with the health care system anywhere from 5–11 times prior to diagnosis, representing missed opportunities for early diagnosis and intervention. New York City remains the epicenter of the HIV/AIDS epidemic in the United States. This study was designed to better understand physician barriers to HIV testing in a large, urban New York City hospital.

Methods: Surveys were distributed to 137 Internal Medicine residents and 47 General Internal Medicine attendings from June 16–August 10, 2005. The survey response rate was 64%.

Results: Internal Medicine Residents reported that they ordered a median of 5 HIV tests over the prior year, while General Internal Medicine attendings reported ordering a median of 8 HIV tests. 41% of residents and 84% of attendings were prompted to order an HIV test if the patient was

MSM. 64% of residents and 81% of attendings were prompted to order an HIV test if the patient had heterosexual contact with an HIV positive person. 96% of residents and 94% of attendings reported that they were comfortable discussing sexual behavior and HIV status; however, only 54% and 81%, respectively, reported initiating risk behavior discussions. More than half of attendings only discussed sexual activity at specific events, and only 10% of attendings reported that they routinely ask about reasons for engaging in risk behaviors. Primary barriers to discussing risk behaviors identified by all respondents included (1) lack of time, (2) more important priorities, and (3) language barriers. 65% of General Internal Medicine attendings and 70% of Internal Medicine residents reported that an intake questionnaire would help facilitate risk behavior discussions.

Conclusion: Physician barriers to HIV testing exist in a large, urban academic medical center. While physicians reported feeling comfortable discussing risk behaviors, time constraints appear to prevent them from translating this into clinical practice. Routine, voluntary HIV testing should be incorporated in large, urban medical settings to avoid missed opportunities to impact the HIV/AIDS epidemic.

Doppler Tissue Systolic Wave Velocity Time Integral, a New Measure of Myocardial Performance. S.G. Jawetz, L.B. Croft, and M.E. Goldman. Mount Sinai Medical Center, New York, NY.

Background: Derivatives of echo-Doppler can assess systolic and diastolic function. The Tei index is a load independent measure of myocardial performance, but requires multiple precise measurements, thereby limiting its general applicability and accuracy. Tissue Doppler imaging (TDI) has primarily been used to measure diastolic function. However, TDI also includes a systolic wave form (S-wave) that indicates total systolic myocardial displacement.

Objective: To determine if measures of the S-wave could serve as a surrogate of the Tei, we correlated the TDI S-wave with the Tei index, and two-dimensional left ventricular function (LVF).

Methods: We blindly, digitally measured the Tei index [isovolumic contraction + isovolumic relaxation/ejection time], S-wave peak velocity, and S-wave velocity-time integral (S-VTI) in 154 random patients' transthoracic echocardiograms. The patients were divided into two groups based on normal or abnormal LV systolic function and were heart rate and blood pressure matched.

Results: The S-VTI correlated with the Tei index ($r = 0.63$, $p < 0.0001$). An S-VTI of 0.015m^2 had a sensitivity of 69% and specificity of 90% to detect an abnormal/normal Tei index. While the S-VTI correlated with the peak S-wave velocity ($r = 0.79$, $p < 0.0001$), the peak S-wave velocity had a poor correlation with the Tei index ($r = 0.29$, $p = 0.0002$). The S-VTI differentiated patients with normal LVF vs. those with moderate or severe LV systolic dysfunction. The sensitivity and specificity of the S-VTI for detecting LV dysfunction was 51% and 96%, respectively; similar to the Tei index (48% and 93%, respectively).

Conclusion: The S-wave VTI is a simple, single measurement of myocardial performance with an excellent correlation with the Tei index.

Mutational Evaluation of NPM-ALK Signal Transduction in the Pathogenesis of Non-Hodgkin Lymphoma. A. Keyzner¹, C. Smith¹, N.H.K. Funato, and D.W. Sternberg. Division of Hematology/Oncology, Mount Sinai School of Medicine, New York, NY. ¹

The t(2;5)(p23;q35) chromosomal translocation juxtaposes the nucleophosmin (NPM) gene with the anaplastic lymphoma kinase (ALK) coding region, and the resulting fusion tyrosine kinase is known to mediate the pathogenesis of some forms of non-Hodgkin lymphoma. We have a limited understanding of signaling pathways that mediate lymphomagenesis driven by NPM-ALK expression. NPM-ALK interactions with signaling proteins are facilitated by protein tyrosine phosphorylation, which binds proteins that contain Src-homology-2 (SH2) or phosphotyrosine binding domain (PTB) motifs. In an effort to identify signaling intermediates that bind NPM-ALK, we tagged the NPM-ALK fusion kinase with the FLAG motif and expressed it in the Ba/F3 hematopoietic cell line. However, we were unable to identify specific interactions on a global scale using anti-PTyr immunoblot or silver staining methods. We speculate that many of the protein-protein interactions are either of low stoichiometry or are transient. In a second effort, we generated a series of Y-to-F substitution mutations within the NPM-ALK kinase. The NPM-ALK variants were used to assess the activity of signaling pathways that might promote cell survival and proliferation. STAT3 is a transcription factor that is known to play a critical role in NPM-ALK-driven lymphomagenesis. We found that a carboxy-terminal triple mutant (Y461F, Y567F and Y644F) attenuates STAT3 activation. Moreover, mutation at these sites impairs the cytokine-indepen-

dent outgrowth of the Ba/F3 hematopoietic cell line. We also found that NPM-ALK could activate the ERK and S6K1 serine/threonine kinases. However, engagement of these downstream signaling molecules could not be localized to a discrete region within NPM-ALK, and we speculate that NPM-ALK signaling through ERK and S6K1 is mediated by promiscuous protein-protein interactions at multiple sites within NPM-ALK. Currently, we are correlating these findings with translational control of gene expression. In conclusion, we find that the domain requirements for STAT3 activation, but not ERK or S6K1 activation, are constrained within the carboxy terminal region of NPM-ALK fusion protein.

Role of the Ubiquitin-Like Protein FAT10 in Renal Epithelial Apoptosis. J-Y Kim. Mount Sinai School of Medicine, New York, NY.

Background: FAT10 is upregulated in several malignancies (particularly hepatocellular carcinoma), autosomal dominant polycystic kidney disease (ADPKD), and HIV-associated nephropathy (HIVAN). In all of these conditions, there is dysregulation of cellular proliferation and apoptosis. While FAT10 is demonstrated to cause proteasome-dependent apoptosis in human and murine cell lines *in vitro*, its function *in vivo* remains unclear. We have previously shown that FAT10 is a critical mediator of HIV-induced apoptosis of kidney cells. However, it is not known whether FAT10 mediates apoptosis due to other proapoptotic stimuli.

Hypothesis: FAT10 is an important mediator of apoptosis in renal epithelial cells exposed to the staurosporine, an inducer of apoptosis.

Methods: Measurement of FAT10 protein expression: HK-2 cells (human proximal tubular kidney cells) were treated for 5 hours with 0.25 μM staurosporine, a chemical known to induce apoptosis via protein kinase inhibition or DMSO (control). Cells were harvested using M-PER protein extraction reagent (Pierce). Insoluble protein fractions were resolubilized in 1% SDS and analyzed by western blotting using rabbit anti-FAT10 affinity purified antibodies.

Analysis of subcellular localization of FAT10: HK2 cells were grown on type 1 collagen-coated coverslips (rat tail collagen, BD Biosciences). Cells were incubated with staurosporine for DMSO control as above and incubated with Mitotracker Red CMXRos for 15 minutes prior to paraformaldehyde fixation. Cells were stained with an affinity purified FAT10 antibody followed by Alexafluor-488 goat anti rabbit antibody secondary antibody, and mounted with DAPI-containing media.

Quantitation of Apoptosis: To determine if inhibition of FAT10 is able to prevent staurosporine induced apoptosis, we transduced HK2 cells with 2 different FAT10 lentiviral shRNA vectors or control shRNA prior to incubation with staurosporine or DMSO. TUNEL staining was performed to assess apoptosis in all cell populations. TUNEL staining was then done in each cell population using the DeadEnd TUNEL staining kit (Promega) and quantified by counting 10 high-power fields per slide.

Results: Western blotting demonstrated a 3.4-fold increase in FAT10 expression in the staurosporine treated cells compared to cells treated with DMSO when normalized with a loading control. Immunocytochemical staining for FAT10 revealed some colocalization with mitochondria and minimal nuclear staining. FAT10 expression was increased in cells treated with staurosporine. There was a suggestion of increased colocalization of FAT10 with mitochondria in staurosporine treated cells. TUNEL staining demonstrated increased apoptosis in the cells treated with staurosporine, but there was no difference in apoptosis observed in cells transduced with shRNA vectors.

Discussion: FAT10 expression was upregulated after treatment of cells with staurosporine and may traffic preferentially to mitochondria after staurosporine treatment. However, knockdown of FAT10 using shRNA did not prevent apoptosis. Additional studies are required to elucidate the mechanisms of FAT10 subcellular localization and function and its role in epithelial apoptosis.

Depressed Patients Are Less Likely to Follow Recommended Risk Reducing Behaviors after Acute Coronary Syndromes. I. Kronish¹, N. Rieckmann¹, E.A. Halm¹ and K. Davidson². ¹Mount Sinai School of Medicine, New York, NY, and ²Columbia University, New York, NY.

Background: The persistence of depressive symptoms after hospitalization is a strong risk factor for mortality after acute coronary syndromes (ACS). Poor adherence to secondary prevention behaviors may be a mediator of the relationship between depression and increased mortality. We aimed to determine whether rates of adherence to risk reducing behaviors were affected by depressive status during hospitalization and 3 months later.

Methods: We enrolled 560 post-ACS patients at 3 university hospitals within 7 days of their coronary event. 492 (88%) patients completed

follow-up at 3 months. We used the Beck Depression Inventory (BDI) to assess depressive symptoms at hospitalization and 3 months later. BDI <10 indicates symptoms of at least mild to moderate depression. We assessed adherence to risk-factor modification behaviors by patient self-report at 3 months. We used χ^2 to compare differences in adherence among 3 groups: patients who were never depressed (BDI < 10 at hospitalization and at 3 months); patients whose depressive symptoms remitted (BDI \geq 10 at hospitalization and BDI < 10 at 3 months); and patients with persistent symptoms of depression (BDI \geq 10 at hospitalization and at 3 months). Multivariate logistic regression was used to calculate adjusted odds ratios controlling simultaneously for pre-specified confounders.

Results: The mean age was 61 years (range 32–93): 41% were female, 11% were Hispanic, and 13% were Black. Among patients who had symptoms of depression during hospitalization, 49% had persistent symptoms at 3 months and 51% had symptoms that remitted. Compared with persistently nondepressed patients, persistently depressed patients reported lower rates of adherence ($p<0.05$) to quitting smoking, taking medications, exercising, and attending cardiac rehabilitation. There were no significant differences in adherence between remittent depressed and persistently nondepressed patients (Table). We next used logistic regression to determine unadjusted and adjusted odds of adhering to recommended behaviors by depression status. Compared with persistently nondepressed, persistently depressed patients reported lower rates of adherence to quitting smoking (adjusted OR 0.23, 95% CI 0.05–0.97), taking medications (adjusted OR 0.50, 95% CI 0.27–0.95), exercising (adjusted OR 0.57, 95% CI 0.34–0.95), and attending cardiac rehabilitation (adjusted OR 0.5, 95% CI 0.27–0.91). Again, there were no significant differences between remittent depressed and persistently nondepressed patients.

Conclusions: Persistently depressed patients were less likely to adhere to behaviors that reduce the risk of recurrent ACS. Differences in adherence to these behaviors may explain in part why depression predicts mortality after ACS.

TABLE
Adherence Behaviors According to Depressive Status

Behavior	Never Depressed	Remitted Symptoms	Persistent Symptoms
Quit smoking	56%	67%	26% ²
Took meds	87%	80%	71% ³
Exercised	60%	55%	37% ²
Cardiac rehab	37%	29%	18% ²
Modified diet	72%	68%	65%

²Significantly different from the other 2 groups (<0.05).

³Significantly different from the persistently nondepressed group (<0.05).

Dysregulation of Hedgehog Pathway Signaling in Hepatocellular Carcinoma. E.R. Lemmer, Y-B Chen, S. Yea, E. Wurmbach, M. Schwartz, G. Khitrov, A. Villanueva, G. Narla, S. Waxman, S.L. Friedman, and J.M. Llovet. Mount Sinai School of Medicine, New York, NY.

Hepatocellular carcinoma (HCC) is a major cancer worldwide whose incidence is rapidly increasing due to end-stage chronic hepatitis C virus (HCV) infection. There is no first line systemic treatment for advanced HCC. Knowledge of the signaling pathways involved in the initiation/progression of HCC will provide a rationale for the design of new molecular targeting agents. In order to characterize the changes in gene expression during the development of HCV-associated HCC, we collected samples from 78 HCV-cirrhotic patients undergoing surgical resection or liver transplantation for HCC. Gene expression of 56 candidate tumor pathway mRNAs were analyzed by real-time RT-PCR in lesions representing six progressive histologic stages (10 normal, 10 cirrhosis, 18 dysplastic lesions, 40 carcinomas) of HCC. Among these, key components of the hedgehog (Hh) signaling pathway, a tumor promoting pathway not previously studied in HCC, were, significantly dysregulated. We found that 24/40 (60%) of HCV-associated HCCs displayed two-fold or more upregulation of *Indian Hedgehog* (*IHH*, Hh ligand) expression compared to 1/28 (3.6%) of cirrhotic livers and dysplastic lesions ($p<0.001$). Concurrently, there was progressive loss of *Human Hedgehog Interacting Protein* (*HHIP*, tumor suppressor) expression with advancing stages of HCC. Human HCC cell lines Huh-7 and Hep-3B showed increased expression of key Hh pathway genes *IHH*, *PTCH*, and *GLI* (similar to very advanced HCCs), indicating Hh pathway activation. In contrast, Hep-G2 (human hepatoblastoma) cells lacked upregulation of Hh pathway genes, while expression of *HHIP* was completely absent in all three cell lines. Inhibition of Hh signaling by the natural alkaloid cyclopamine (dose 10 μ M) resulted

in decreased ³H-thymidine incorporation by Huh-7 (by 23%) and Hep-3B (by 53%) cells, but not by Hep-G2 cells. In contrast, tomatidine (dose 10 μ M)—a compound with a similar structure to cyclopamine but which lacks its inhibitory effects on Smo—had no effect on the proliferation of HCC cell lines. In conclusion, (1) Activation of the Hh pathway occurs in a subgroup of human HCV-cirrhotic HCCs; (2) Tumor growth in these patients appears to be ligand driven, and upregulation of *IHH* expression may be a critical molecular switch during the step-wise progression to HCC; and (3) Growth of human HCC cell lines displaying upregulation of Hh pathway gene expression appears to be inhibited by Hh pathway blockade.

Examining Physician Opioid-Prescribing Practices for Older Adults—A Retrospective Analysis. E. Littrivis. Mount Sinai School of Medicine, New York, NY.

Background: Studies suggest that older adults are at high risk for undertreatment of pain and that they receive less analgesia for the same level of pain than their younger counterparts.

Objective: To examine physician practices of analgesic prescribing across different age groups.

Setting: Tertiary Care Academic Hospital.

Patients: A total of 1,115 patients, ages 18–75 years and older, enrolled in a study to examine a series of interventions designed to increase assessment and knowledge of pain. Patients were included if they were not taking opioids as an outpatient, did not have a history of liver disease, reported moderate to severe pain on the day of admission, and remained hospitalized for at least 72 hours.

Methods: Subjects were enrolled within 48 hours of admission to 9 matched medical and surgical units. Trained research assistants interviewed patients on a daily basis and asked them to rate their current pain, worst pain, and pain relief with analgesics on numeric rating scales. Patients were also queried as to opioid-related side effects including nausea, sedation, pruritus, and mental clarity.

Main Outcome Measures: Average pain at rest, worst pain over prior 24 hours, pain relief with analgesics, and prevalence of opioid related side effects.

Analyses: ANOVA and chi-square tests were used to compare continuous and discrete variables. Multivariate linear and logistic regression was used to examine outcome measures adjusting for covariates.

Results: There were statistically significant differences in the mean morphine equivalents administered amongst the different age categories and amongst surgical and medical pain management regimens overall. Amongst patients 18–49 years of age, the mean opioid dose required to achieve adequate pain relief was 50 morphine equivalents as compared to 21 morphine equivalents amongst patients 75 and older. Surgical patients in total received almost double the amount of morphine equivalents (186 versus 96) as compared to medical patients over a 5-day follow-up period. While older patients received less morphine equivalents than their younger counterparts, they overall achieved an equal amount of pain relief. Approximately 50% of all patients in each age category received adequate pain relief as defined as a pain score decrease from moderate—severe pain on hospital admission to mild—no pain by days 3–5.

Amongst all patients who reported moderate—severe pain at study entry and received an opioid, side effect profiles were also reported and recorded. No significant difference was observed among side effect profiles when comparing older adults to their younger counterparts.

Conclusions: Older adults require less analgesia for the same amount of pain relief as compared to younger adults without a significant difference in side effect profiles.

Phase I Study of Rituximab-Cyclophosphamide (R-CY) Stem Cell Mobilization and Rituximab-BEAM HDC with ASCT in Patients with Relapsed, Refractory or High Risk Intermediate Grade Non-Hodgkin's Lymphoma. A. Malone¹, E. Scigliano¹, C. Grosskreutz², S. Fruchtman³, J. Gabrilove¹, J. Mandeli², and L. Isola¹. ¹Division of Hematology-Oncology and ²Department of Biomathematical Sciences, Mount Sinai Medical Center, New York, NY and ³Tibotec Therapeutics, Bridgewater, NJ.

The addition of rituximab to mobilizing regimens does not adversely affect collection of adequate numbers of CD34+ PBSC and may decrease tumor cell contamination. Prior administration of rituximab may sensitize lymphoma cells to chemotherapy, but its use with high-dose chemotherapy has not been studied. In this study, eligible patients had intermediate grade non-Hodgkins lymphomas (NHL) either primary refractory, relapsed or in CR-1 with an intermediate/high risk IPI score. Eight patients with a median age of 49 years (28–61) were enrolled in this study. Four patients

had relapsed disease, chemosensitive to salvage in 3 patients, and untested in 1 patient. Two patients had primary refractory disease, chemosensitive to salvage. Two patients had intermediate-high risk IPI scores and were in CR-1. One patient in CR-1 declined to undergo transplant following stem cell collection. All patients had received rituximab previously. Stem cell mobilization was rituximab 375 mg/m² followed by CY 2 gm/m²/day for 2 doses and filgrastim 10 ug/kg/d. High-dose chemotherapy consisted of rituximab 375 mg/m² on day-8, carmustine 300 mg/m² on day-7, etoposide 200 mg/m²/d on days -6 to -3, cytosine arabinoside 200 mg/m² on days -6 to -3 (8 doses) and melphalan 140 mg/m² on day -2. Patients received filgrastim post transplant.

Results: The median CD34+ cell dose collected was 12.5 × 10⁶/kg (1.1 – 33.2). There was one inadequate CD34+ cell collection requiring bone marrow harvesting which yielded 0.72 × 10⁶/kg CD34+ cells. Engraftment of neutrophils and platelets occurred at a median of 8 and 11 days post transplant, respectively. Infectious complications included febrile neutropenia in one patient following mobilization and in 6 patients following R-BEAM. Transient grade I-II (common toxicity criteria) hepatic enzyme elevation occurred in 2 patients following R-CY. Following R-BEAM, 3 patients developed grade II-IV LFT elevation without evidence of VOD, which resolved. One patient developed moderate hemorrhagic cystitis which resolved. One patient developed bilateral pulmonary infiltrates of unknown etiology (BAL negative for organisms) which resolved. Immunoglobulin levels remained normal in two patients, but decreased in all other patients for up to a year post transplant. Peripheral blood flow cytometry and T cell subset analysis showed absent B cell populations, decreased CD4 cells and increased CD8 cells in all patients up to a year post transplant. Five patients are alive with no evidence of disease 381 – 676 days after transplant. Three of these patients developed PET positive lymph nodes that showed florid follicular hyperplasia on biopsy, with no evidence of lymphoma. Two patients had persistent disease following transplant. One patient underwent a non-myeloablative allogeneic transplant and died of progressive disease.

Conclusions: R-CY was well tolerated as a mobilization regimen and led to adequate stem cell collection. The addition of rituximab to the high dose chemotherapy regimen did not appear to increase the incidence of infections or peritransplant complications in this Phase I study. The effect on disease free survival, or the addition of rituximab to the collection and preparative regimens requires further investigation.

Assessing the Immunosuppressive Effects of 6MP/Azathioprine in IBD. L. Malter. Mount Sinai School of Medicine, New York, NY.

Background: Azathioprine/6 mercaptopurine (AZA/6MP) are immunomodulatory agents that are used for the treatment of immune mediated inflammatory diseases and transplant rejection including inflammatory bowel disease (IBD). In IBD, the indications for its use include disease refractory to treatment with 5ASA and steroids, as a steroid sparing agent, in conjunction with anti-tumor necrosis factor α mAb, or in the treatment of fistulizing Crohn's disease. The dose of AZA/6MP used in IBD is lower than that used to treat malignancy or transplant rejection where greater immunosuppression is required. The majority of studies evaluating the immunosuppressive effects of AZA/6MP have been conducted in patients taking higher doses. The goal of this study is to evaluate the effect of AZA/6MP on humoral and cellular immune responses in IBD patients, both *in vivo* and *in vitro*.

Methods: Twenty patients with Crohn's disease or ulcerative colitis diagnosed by colonoscopy and confirmed by biopsies or small bowel radiograph and non-inflammatory controls are studied prospectively following the initiation of 6MP/AZA therapy. Venous blood is obtained prior to starting 6MP/AZA and after 3 and 6 months of therapy. Lymphocyte counts, *in vitro* response to antigen (Candida and Tetanus) and mitogen stimulation (Con A, PHA, PWM), and total and IgG subclass immunoglobulins are determined. Response to pneumococcal, tetanus, influenza and Hemophilus influenza B vaccinations are analyzed as well. We analyzed values using stimulation indices to normalize lymphocyte proliferation in response to various stimuli.

Results: We are presenting an interim analysis of 17 patients recruited thus far. We initially compared the *in vitro* response to antigen and mitogens prior to receiving treatment in IBD patients vs controls. The patient response to all stimuli was comparable to controls confirming there was no baseline immunosuppression in IBD patients. Following treatment, the response to PHA trended to be lower but the response to Con A and PWM remained stable. Similarly, the response to Candida and Tetanus was unchanged in the setting of 6 MP therapy. Lastly, the percent CD4 count was unchanged in treated patients.

Conclusions: The data to date support the contention that therapy with azathioprine/6 mercaptopurine, at doses used in the treatment of IBD, does not suppress systemic immune responses *in vitro*.

Serum Vascular Endothelial Growth Factor (VEGF) and Hepatocyte Growth Factor (HGF) Are Increased following Transarterial Chemoembolization (TACE) in Unresectable Hepatocellular Carcinoma (HCC). J.D. Schwartz, M.C. Marcotrigiano, Q. Zuo, and J.L. Gabrilove. Mount Sinai School of Medicine, New York, NY.

Background: TACE prolongs survival in unresectable HCC; tumor recurrence is nonetheless frequent and TACE is rarely curative. HCC is a vascular neoplasm in which aberrant cytokine pathways likely contribute to growth and angiogenesis. We sought to characterize the clinical course of HCC patients undergoing TACE and to determine potential association between TACE and levels of circulating VEGF and other cytokines.

Methods: We measured circulating VEGF, HGF, basic fibroblast growth factor (bFGF), tumor necrosis factor (TNF)-alpha, and transforming growth factor (TGF)-alpha in the serum of 38 patients undergoing TACE; cytokines were measured pre-treatment, and at days 1 and 2, and weeks 1, 2 and 4 following TACE. All patients were followed for HCC progression and survival.

Results: A total of 38 HCC patients underwent TACE. Median age was 57 (21 – 80); 30 patients were male; 30 had HCV-related liver disease; 34 had ECOG PS 0 – 1; 19 had Child-Pugh Class A liver dysfunction; median tumor diameter was 3.6 cm (1.3 – 9.6 cm); median number of tumors was 3; 8 patients had unifocal tumor and 14 had \geq 5 tumors. Median time-to-progression was 7 months (range 1 – 40+), excluding 5 patients who died of progressive hepatic failure or complications secondary to TACE or liver transplant (OLT) within 6 months. Median overall survival (OS) was 12 months (range: 2 – 40+). Frequent toxicities included nausea (76%; 24% grade 3), pain (71%; 16% grade 3) and fatigue (68%); serious toxicities included grade 4 GI bleeding (5%), hemoperitoneum (3%) and jaundice (4%). Mean circulating VEGF was elevated from a baseline of 229 pg/mL (standard error (SE) 56) to 600 pg/mL (SE 166) at 1 week following TACE and decreased to baseline levels at 4 weeks. Serum HGF was elevated from baseline (1,712 pg/mL; SE 250) to 2,847 pg/mL (SE 523) at 2 days following TACE and also returned to baseline at 4 weeks. Serum bFGF, TNF-alpha and TGF-alpha were not significantly elevated from baseline following TACE.

Conclusions: TTP and OS vary widely in patients with unresectable HCC following TACE. Both HGF and VEGF are significantly elevated following TACE. We are currently investigating potential association between elevation of these cytokines and clinical features and outcomes.

Subspecialty Evaluation of Chronically Ill Patients with Suspected Immune Defects. A. Mehra*, P. Sidi#**, J. Doucette+, L. Estrella**, and C. Cunningham-Rundles**. Mount Sinai School of Medicine, New York, NY.

Background: The diagnosis of primary immunodeficiency is suggested by illnesses including recurrent, unusual, or persistent infections. Since the diversity of defects and clinical presentations present a diagnostic challenge in large hospital populations, we devised a computer algorithm to identify such patients.

Objective: To determine the patterns of medical care rendered to patients with clinical features of immunodeficiency and assess utilization of pertinent sub-specialty clinics.

Methods: Using a validated algorithm based on disease codes from the International Classification of Disease (ICD-9), applied to Mount Sinai Hospital billing records, we identified all hospitalized patients, age 60 years or less who had been given two or more of 174 diagnoses of illnesses often associated with immunodeficiency. ICD codes were weighted for severity and expressed as a sum for admissions between 1/1/99 and 12/31/03; records of subjects with scores of 6 or greater were studied. Demographic and clinic attendance were assessed using billing records.

Results: The 296 computer-identified patients were 36% Hispanic and 27% African American with a median age of 13.3 years. Twenty-six percent live in the hospital's zip code; 75% receive primary care at Mount Sinai. Patients were hospitalized a median of 4.2 times (range 1 to 42). While 81% of the subjects had 402 episodes of pneumonia, only 169 subjects (55%) had ever received an evaluation from Allergy/Immunology or Pulmonary services.

Conclusion: Despite receiving primary medical care at one hospital, frequently hospitalized subjects with clinical features of immunodeficiency do not receive medical care in appropriate subspecialty clinics.

Identification of a Retrovirus in Human Breast Cancer. S.M. Melana, I. Nepomnaschy, M. Saskalian, H. Rojowsky, A. Abbott, J. Hasa, J.F. Holland, and B. G-T Pogo. Hematology / Oncology Division, Department of Medicine, Mount Sinai School of Medicine, New York, NY.

We have previously reported sequences homologous to the *env* gene of Mouse Mammary Tumor Virus (MMTV) but not to human endogenous retroviruses in 38% of the human breast cancers studied, yet they were absent from others human tissues (Wang et al, Cancer Res 1995, 55:5173). We have also found that normal breast tissue from *env* positive breast cancer patients was negative, suggesting that the sequences are of exogenous origin (Melana et al. *Cl Cancer Res* 2001, 7:283). The sequences were also expressed in most of the positive breast cancer specimens as detected by reverse transcriptase (RT) PCR (Wang et al. *Cl Cancer Res* 1998, 4:2565). Finally, the complete 9.9 Kb proviral sequence of an MMTV-like agent has been amplified and sequenced in two breast cancers (Liu, B. et al. *Cancer Res* 2001, 61:1754). Structural features of this provirus suggest that it is functional. We have looked for the presence of viral particles in primary cultures (MSSM cells) of *env* sequence positive tumors. The cells expressed Env proteins as shown by immunofluorescence and western blot. FACS analysis indicated that between 10–20% of the cells expressed the surface protein. Retroviral particles budding from cells as well as in particulate fractions from culture media were observed by electron microscopy. Particulate fractions also display reverse transcriptase (RT) activity and the presence of all viral genes as detected by RT-PCR. The RT activity peaked at densities characteristic of retroviruses in sucrose gradients. None of these properties were observed in similar studies with normal human mammary epithelial cells (HMEC) primary cultures or established normal breast cell line (MCF10F). Co-culture of MSSM virus-producing cells with HMEC, MCF10F, and B cells (Ramos) demonstrated transfer of viral sequences, as detected by PCR, and expression of Env proteins by western blot and FACS analysis in the recipient cells. Taken together, these findings support the identification of a human mammary tumor virus (HMTV) similar to MMTV in human breast cancer, which is able to infect human cells. Morphological cell transformation and tumorigenesis experiments are being performed.

The Frequency of *FAT10* Alleles in Renal Transplant Recipients. S.A. Mesher, C.M. Wyatt, B.T. Murphy, B. Schroppel, and M. J. Ross. Mount Sinai School of Medicine, New York, NY.

Background: Many factors affect outcome in renal transplant recipients, including genetic and environmental factors. *FAT10* is a ubiquitin-like protein that has been shown to be upregulated in patients after infection with HIV-1, and is capable of inducing apoptosis in human renal tubular epithelial cells. Four distinct alleles of *FAT10* have been identified (*FAT10^{a-d}*), with one allele (*FAT10^b*) noted to be more prevalent in patients with HIV associated nephropathy (HIVAN). We tested the hypothesis that particular *FAT10* alleles are associated with conditions leading to end stage renal disease (ESRD) and with renal transplant outcome.

Methods: The *FAT10* gene was amplified and sequenced from genomic DNA from 83 renal transplant recipients. Chi-square analysis was used to test the association between each *FAT10* allele and several variables, including demographic data (race, sex), predisposing conditions (hypertension, diabetes, other disease), and transplant outcomes (total rejection episodes, fewer than 2 rejection episodes, and post-transplant creatinine clearance at 1 and 5 years). We also compared the prevalence of alleles (stratified by race) in our population with allele frequencies derived from a single nucleotide polymorphism (SNP) database (dbSNP, www.ncbi.nlm.nih.gov) using Fisher's exact test.

Results: A total of 83 DNA samples were analyzed (166 alleles) in 28 Caucasians, 22 African Americans (AA), and 28 Hispanics. Frequencies were calculated for each *FAT10* allele. Of 166 alleles, there were 102 alleles of *FAT10^a* (frequency 0.61), 38 alleles of *FAT10^b* (frequency 0.23), 0 alleles of *FAT10^c* (freq 0.0), and 26 alleles of *FAT10^d* (frequency 0.16). The *FAT10^b* allele was significantly associated with AA race ($p < 0.001$). There was no statistically significant difference in predisposing conditions, transplant outcome or creatinine clearance at 1 and 5 years among the various groups. The prevalence of the *FAT10^c* allele in the transplant recipient cohort was significantly lower than has been reported in other cohorts of similar racial background ($p < 0.0001$).

Conclusions: No association was detected between *FAT10* alleles and outcome after renal transplant in this study. We cannot rule out, however, that an association was missed due to our limited sample size. The absence of the *FAT10^c* allele was noteworthy, as published SNP data have shown its frequency in the general population to be 25% in Caucasians and 3% in Africans. The *FAT10^c* allele may be associated with resistance to chronic kidney disease, and further study should be undertaken looking for the allele in a chronic kidney disease population.

Internal Medicine Housestaff Experience with Interdisciplinary Team Work on the ACE Unit. R. Kellerman Miller, and E. Callahan. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

Objectives:

1. Assess Mount Sinai Internal Medicine Housestaff ("Housestaff") attitudes toward and knowledge of interdisciplinary teams (IDT) and the roles of members of an interdisciplinary team.
2. Assess Housestaff experience with interdisciplinary teamwork.
3. Evaluate the effect of a 4-week rotation on the geriatric medical service towards the attitudes of Housestaff on interdisciplinary teamwork.

Description of Educational Project: Housestaff rotate for 4 weeks on the Acute Care for the Elderly (ACE) Unit and are expected to function as members of the IDT. Dedicated interdisciplinary rounds are scheduled daily and Housestaff are expected to attend two times per week. During their ACE orientation, Housestaff were given a description of their role in interdisciplinary rounds and principles of interdisciplinary rounds. Each rotation also included a 1/2-hour educational session with the geriatric nutritionist and physical therapist. Pre- and post-rotation surveys were distributed and collected by the authors.

Evaluation: At the start of their rotation, we used four-point Likert scales to assess Housestaff's attitudes toward IDT, knowledge of other disciplines, and previous experiences in IDT. At the end of their rotation, we asked similar questions. In addition, we asked if their attitudes changed after the four weeks.

Discussion: Preliminary results:

1. Pre-rotation attitudes were very positive overall. The higher-than-expected baseline signifies a change in the overall attitudes of Housestaff when compared to the Geriatrics Interdisciplinary Team Training (GITT) study (Leipzig, JAGS, 2002).
2. Prior to rotation, Housestaff reported greater knowledge of the roles/responsibilities of nurses/social workers versus nutritionist/physical therapists.
3. Most of the Housestaff had prior experience with IDT in medical school and residency.
4. ACE rotation had very little effect on the attitudes of Housestaff and their knowledge of IDT. Full results to be presented.

Conclusions: Housestaff are being trained in a manner more solicitous of interdisciplinary teamwork. They are therefore entering their post-graduate training with a more positive attitude toward such teamwork based on these experiences. We think that the ACE Unit rotation was not very influential in their attitudes because they began their rotation with a very positive attitude, only PGY 2 and 3 were expected to attend IDT rounds, and some of the structure of the rounds was lost due to changes in their rotation.

In the future, housestaff involvement with IDT could be incorporated into other educational methods such as role-plays and case based discussions, with accompanying "Team Assessment tools" in addition. Focus groups with both the housestaff and other team members may help investigate different ways to improve housestaff experiences in an interdisciplinary teamwork.

Desmoid Tumors: Looking for a Cause and a Cure. F.P. Noto. Mount Sinai School of Medicine, New York, NY.

Desmoid tumors (DTs) are benign proliferation of fibroblasts which by virtue of their local aggressiveness and interference with the functioning of adjacent organs can produce significant morbidity and mortality. DTs are rare tumors with an incidence of 0.37 per 100,000 per year. DTs however occur in up to 20% of patients with familial polyposis syndromes, the genetics of which may offer a lead into the molecular pathogenesis of uncontrolled fibroblast proliferation disorders. The dysregulated expression of the beta-catenin gene has been associated with DTs and may offer a target for the development of therapeutic interventions. Currently, the standard treatment for DTs is surgical resection, but complete resections are rare and recurrences common. Other modalities which have been attempted include radiation therapy, noncytotoxic and hormonal therapy as well as cytotoxic chemotherapy. Cures with current treatment modalities are rare and the investigation of the cause of DTs may offer the best hope for a curative intervention in the future.

Cortistatin Modulates Immune Responses and Is Deficient in Lamina Propria Mononuclear Cells from Inflammatory Bowel Disease (IBD) Patients. S.J. Brown, Y. Zheng, P. Ponda, L. Mayer, K. Patel, and M. Babyatsky. GI Division and Shared Research Facility, Mount Sinai School of Medicine, New York, NY.

Background: Cortistatin (CST) is a novel neuropeptide, homologous to somatostatin (SST) in its receptor binding domain. Intestinal SST expression is decreased in IBD (*Gastroenterology* 1996; 110:A957) and SST has been ascribed immunomodulatory properties. New data indicates CST, and not SST, is actually expressed by cells of the human immune system (Dalm V, *Clin Endo* 2004; 60:625) suggesting CST may play a more significant role as an autocrine or paracrine immune regulator. We examined biopsies from ulcerative colitis and Crohn's colitis patients (n=9) and non-inflamed controls (n=18) for CST mRNA expression and determined the immunomodulatory effect of CST on macrophage hybridoma cells (clone-63) and Jurkat cells.

Methods: Lamina propria mononuclear cells were isolated and mRNA extracted. Q-PCR was performed using CST-specific primers with rps-11, β -actin and α -tubulin serving as housekeeper genes. Non-stimulated cell lines were treated with human CST-17 at 0.1 and 1 μ M for 1, 4, and 16 hours. mRNA was harvested and RT-PCR for interleukin (IL)-12p40, IL-10, IL-13, interferon γ (IFN γ), IL-4, TGFB was performed using a MPCR kit (Maxim BioTech). Expression levels were determined relative to GAPDH housekeeper gene.

Results: Cortistatin expression was reduced in IBD samples with a mean value of 9.10 U (\pm 2.24 SEM) compared to 127.9 U (\pm 56.1 SEM) for normal controls ($p=0.004$ Mann-Whitney). This difference appeared to apply to both active and inactive disease and to both Crohn's and ulcerative colitis.

CST treatment of clone-63 cells led to a 1.6–4.1-fold inhibition of IL12p40 production. IFN γ production was also inhibited up to 2.7-fold in a time and dose dependent fashion. A mild, 1.5-fold increase in TGFB production was also seen. CST treatment of Jurkat cells led to a 1.7-fold inhibition of IFN γ production that was time and dose dependent. No significant change in the expression of other examined cytokines was detected.

Conclusions: We demonstrate for the first time that (1) CST expression is reduced in lamina propria cells from IBD patients and (2) CST displays immunomodulatory properties. Altered CST expression may contribute to the pathogenesis of IBD and CST may prove to be a novel therapeutic peptide.

Loneliness and Partner Status Are Associated with Poorer Adherence to Recommended Health Behaviors after Acute Coronary Syndromes. M. Paz-Yepes¹, N. Reichmann², I. Kronish³, M.M. Burg⁴, J.E. Schwartz², and K.W. Davidson⁴. ¹Cardiovascular Institute, ²Psychiatry, and ³Medicine, Mount Sinai School of Medicine, New York, ⁴Medicine, Columbia University, New York, NY; and ⁵Psychiatry, Stony Brook University, Stony Brook, NY.

Social isolation predicts pathogenesis of coronary artery disease, possibly because of poor health behaviors. We previously reported that depression is associated with poorer health behaviors after an acute coronary syndrome (ACS). Here, we examined whether social isolation, defined by not having a partner and perceived loneliness, is associated with health behaviors independent of depression.

We enrolled 560 patients within 7 days of an ACS. A total of 492 patients (88%) completed follow-up at 3 months. Partner status, the UCLA loneliness scale (6-items), and the Beck Depression Inventory (BDI) were assessed at baseline. Self-reported health behaviors were assessed at 3 months. Patients without a partner (n=174, 35%) scored marginally higher on the UCLA scale than those with a partner (M=2.0, SD=0.7 vs. M=1.9, SD=0.5, $p=0.13$). Scores on the UCLA scale and BDI were moderately correlated ($r=0.54$, $p<0.001$).

After 3 months, patients without a partner were less likely to participate in cardiac rehabilitation (35% vs. 64%, $p=0.01$) or exercise (46% vs. 57%, $p=0.03$), and were more likely to smoke (15% vs. 8%, $p=0.01$). There were no group differences in self-reported medication adherence and diet change ($p>0.20$).

UCLA score was associated with decreased medication adherence ($r=-0.21$, $p<0.01$), lack of exercise ($p=0.02$), and a greater likelihood of smoking ($p=0.02$). Hierarchical regression analyses including age, gender, UCLA score, partner status and depression as predictors showed that both UCLA score and not having a partner, but not depression, were associated with smoking. Depression, but not UCLA score or partner status, was significantly associated with decreased likelihood of cardiac rehabilitation or exercise participation, and decreased medication adherence (all $p<0.05$).

These data suggest that social isolation, defined by not having a partner and perceived loneliness, should be considered when improvement in health behaviors is needed after acute coronary syndromes. Social isolation is associated generally with health-damaging behavior, whereas depression is associated with a decreased engagement in physical activity and medication adherence. Differential treatments may be implicated for socially isolated vs. depressed patients.

Efficacy of a Clinical Feedback Form in Improving Feedback in Medical Education. L. Peccoralo¹, K. Arbatova¹, E. Friedman, L. Bensinger, and J. Koestler. Mount Sinai School of Medicine, New York, NY. ¹Co-first authors.

Introduction: Medical education literature highlights the distinction between the evaluation of clinical performance at the end of a clerkship and the feedback given by faculty to students throughout a clerkship. Feedback improves clinical skills and increases student self-awareness throughout medical education. In fact, it has been shown that the best educators consistently use feedback as part of their teaching. However, not all feedback is considered useful. Valuable feedback should include an assessment of a student's strengths and weaknesses and specific ways in which to improve clinical skills. Despite what we know about the importance of feedback, it is still lacking in quantity and quality throughout clinical education.

Hypotheses: We hypothesize that students are unsatisfied with the feedback that they currently receive in the third year. In addition, there are specific barriers to giving effective feedback that we can identify. Finally, we hypothesize that a written clinical feedback form will facilitate supervisors giving feedback in medical school clerkships at Mount Sinai School of Medicine (MSSM).

Methods: We first assessed satisfaction with and barriers to feedback using separate questionnaires tailored to students and their supervisors (residents). The first set of questionnaires were administered in July and August of 2005 and included specific questions regarding qualities of good feedback, satisfaction with feedback received or given, and barriers to adequate feedback. In order to improve feedback given in clinical clerkships we developed a concise clinical feedback form that students give to their supervisors throughout the third year clinical clerkships. The form is intended to be a guide for a feedback encounter between a student and his/her supervisor (usually a resident). The efficacy of the form will be evaluated by administering additional questionnaires to the students, residents, and faculty that used the forms. The study will be completed at the end of the 2005–2006 academic year.

Preliminary Results: Preliminary data demonstrates that there is a consensus between medical students' and residents' perception of the importance of feedback in clinical education. A large proportion of residents reported giving insufficient feedback, while a large proportion of medical students reported receiving inadequate feedback during their clerkships. Specific barriers to adequate feedback were noted by both medical students and residents. We will assess whether some of these barriers are addressed by our current intervention and hope to identify future interventions that will improve the quality of feedback for students at MSSM.

Medication Beliefs Predict Adherence to Inhaled Steroids in Inner City Asthmatics. D. Ponieman¹, J.P. Wisnivesky¹, H. Leventhal², and E.A. Halm¹. ¹Mount Sinai School of Medicine, New York, NY, and ²Rutgers, The State University of New Jersey, New Brunswick, NJ.

Background: Asthma morbidity, mortality, and health services utilization is highest among inner-city populations. Adherence to daily inhaled corticosteroids (ICS) therapy is the cornerstone of evidence-based asthma management. However, adherence is often suboptimal. Several domains of medication beliefs may influence adherence with ICS including beliefs about necessity/importance, concerns, self-efficacy, and regimen complexity, among others. This study sought to examine a range of medication beliefs and their association with adherence to ICS.

Methods: Detailed sociodemographic, clinical, and health belief data were collected in a prospective, observational cohort of inner city adults with persistent asthma in English and Spanish. Medication beliefs were based on Self-Regulation Theory and previously developed instruments. Beliefs about necessity related to importance of using ICS when symptomatic (SX) and when asymptomatic (ASX). Concern items related to worries about side effects and addiction. Other items include: "confidence in ability to use ICS (self-efficacy), and "how hard to follow your medication schedule (regimen complexity). Self-reported adherence to ICS was assessed using: (1) the Medication Adherence Reporting Scale (MARS), a validated, 10 item tool

measuring overall adherence to ICS (Cronbach's alpha=0.83), and (2) questions about frequency of use of ICS when SX and when ASX. Associations between beliefs and ICS adherence was assessed using Spearman correlations and chi square tests. Multivariate (MV) analyses adjusted for other factors known to influence adherence (age, sex, and asthma severity).

Results: Of the 204 patients (Pts), mean age was 48 yrs, 60% Hispanic, 30% Black, and 20% completed the survey in Spanish. Overall, 10% had prior intubation, 57% prior asthma hospitalizations, and 71% had used oral steroids; 85% were prescribed ICS. Among these Pts, they reported using their ICS all/most of the time more often when having SX v. ASX (74% v. 68%, $p<0.0005$). In univariate analyses, medication adherence (MARS score) was associated with beliefs about the importance of using ICS when ASX, worries about addiction and side effects, confidence in using ICS, and regimen complexity ($p<0.05$). In MV models that adjusted for age, sex, and asthma severity, beliefs about importance of using ICS when ASX, worries about addiction, and confidence in using ICS remained significant predictors of medication adherence (MARS). In stepwise MV models that considered all beliefs together, beliefs about the importance of using ICS when ASX and confidence in using ICS were independent predictors of overall adherence adjusting for age, sex, and severity ($p<0.05$). As predicted by the conceptual model (in univariate and MV models), beliefs about the importance of use of ICS when ASX were correlated with use of ICS when ASX ($p<0.0001$), but not ICS use when SX ($p=0.3$). Similarly, beliefs about importance of using ICS when SX were associated with adherence when SX ($p<0.0001$), but not adherence when ASX ($p=0.5$). Greater worries about addiction to ICS were associated with less frequent use of ICS when SX and ASX ($p<0.005$).

Conclusions: Several key positive and negative beliefs about medications were associated with several measures of adherence to ICS. Eliciting and addressing these underlying beliefs may help improve adherence and outcomes. These potentially modifiable beliefs are promising targets for future asthma self-management interventions.

Simplified Insulin Drip Protocol for Patients with ACS Admitted to a Cardiac ICU. M. Ryan. Mount Sinai School of Medicine, New York, NY.

Objective: To assess the effectiveness of a simplified insulin drip protocol on patients admitted to a cardiac intensive care unit with symptoms of acute coronary syndrome.

Patients: This study is a case series of 14 patients admitted to the Mount Sinai Hospital Cardiac Care Unit from June through October 2005. All patients had either known diabetes or were found to have a plasma glucose of greater than 200 on admission to the CCU. The average age in the study group was 70.1 years with a range from 54 to 86.6 of the subjects were women and 8 were men. The study group included the following ethnicities: Caucasians, Asians, South Asians, African Americans and Hispanics. The average BMI in the study group was 28.4 (23–38) and the average baseline HbA1C was 8.57. The majority of patients also had hyperlipidemia and hypertension and 4 of the study patients were on hemodialysis for renal failure.

Methods: The insulin drip protocol was to be initiated in patients with diabetes or with blood glucose > 200 mg/dL admitted to the CCU within 48 hours of the onset of acute coronary syndrome. The goal was to maintain patients within a blood glucose range of 81–140 mg/dL. The initial rate of the insulin drip was determined by the patient's starting blood glucose level and the rate was adjusted based on repeat blood glucose measurements.

Results: Of the 14 patients in the study, 9 reached the goal blood glucose range of <140 within 4 hours of initiation of the drip. The average blood glucose level for patients while on the drip was 156mg/dL. There were no incidences of significant hypoglycemia (defined as blood glucose <40 mg/dl) in any patients during this study.

Conclusions: This simplified insulin drip protocol is effective in lowering and maintaining blood glucose levels and is very safe. Despite the common fear of hypoglycemia in patients on an insulin drip, its incidence in this small study was extremely rare.

A Patient Navigator (PN) in an Open Access Endoscopy (OAE) Program Facilitates Completion and Satisfaction with Screening Colonoscopy (SC) among Low-Income Underrepresented Minorities (URMs). S. Santos, L. Jandorf, S. Itzkowitz, A. Castillo, and J. Christie. Mount Sinai School of Medicine, New York, NY.

Background: African Americans and Hispanics have lower screening rates for colorectal cancer (CRC) than Caucasians. Organizational barriers such as lack of patient (pt) access to timely referrals, adequate follow-up and reminder systems have an impact on successful CRC screening. OAE

is becoming more common in the United States. The advantages of OAE include shorter waiting times, better control by referring physicians over pt management for preventive services, and lower costs and inconvenience by eliminating an initial gastrointestinal consultation.

Aim: To assess pt satisfaction with the SC process in an OAE program.

Methods: Average risk, asymptomatic URMs from the primary care clinic at Mount Sinai Hospital were referred for SC through OAE. The majority of pts reside in East Harlem, a medically underserved community. The role of the PN included pt education, explanation of bowel preparation, scheduling appointments, assisting with transportation/escorts, and providing counseling and support to pts. After referral, the PN contacted each person to assess appropriateness for OAE and discuss the procedure and bowel prep. Two weeks after SC, pts were contacted by phone to conduct a 19-item patient satisfaction survey.

Results: From June–Oct 2005, 120 people completed their SC and 106 completed the pt satisfaction survey (response rate: 88%). 85% were female. 56% were Hispanic, 29% African-American and 11% Caucasian. The mean age was 56.2 (SD= 5.2). 84.2% stated that their primary care provider (PCP) adequately explained the reason for the SC. After contact with the PN, this rate increased to 92.1% ($p=0.02$). 34.9% of pts were extremely satisfied with their PCP's explanation of the bowel prep in comparison to 58.5% following the PN explanation ($p=0.00$). 83% were extremely satisfied or satisfied with PCP explanation of bowel prep versus 99.1% after PN explanation ($p=NS$). 94% of pts were extremely satisfied/satisfied with the SC procedure itself, and 89% were extremely satisfied/satisfied with the sedation during the procedure. Only 2% of pts were dissatisfied with the quality of services received during the SC program. 10% of pts were extremely dissatisfied or dissatisfied with how the results were explained after the procedure. Importantly, 64% of participants said they would not have completed the SC without the assistance of the PN.

Conclusions: PN, in an OAE program among low-income URMs, helps pts overcome barriers to SC. Nearly two-thirds of pts would not have undergone a SC without PN assistance. Overall, pts were highly satisfied with the SC program. APN program may help reduce racial disparities in CRC screening.

Depression following Acute Coronary Syndrome Is Not Associated with the GRACE 6-Month Mortality Index. D. Schwartz. Mount Sinai School of Medicine, New York, NY.

Background: Depression has been shown to be associated with increased mortality following hospitalization for acute coronary syndromes (ACS). While some researchers have argued that this association is a result of a biobehavioral mechanism linking depression with post-ACS mortality, others have argued that analyses linking depression with mortality failed to properly control statistically for cardiac disease severity. The measures thus far utilized to account for cardiac status have been varied and have not been validated to predict post-ACS mortality. We sought to assess whether cardiac severity could be a confounder of the relationship between depression and post-ACS depression by testing whether there was an association between depressive symptoms and the Global Registry of Acute Coronary Events (GRACE) score, a validated prediction model used to predict 6-month mortality after ACS.

Methods: A total of 457 post-ACS patients were enrolled within 7 days of their coronary event at 2 university hospitals. 413 (90%) completed follow-up at 3 months. The Beck Depression Inventory (BDI) was used to assess depressive symptoms at hospitalization. A BDI score ≥ 10 indicates symptoms of at least mild depression, while a score of 0–4 indicates minimal to no depression. The Depression Interview with Structured Hamilton (DISH) was used as an additional measure of depression at hospitalization. At 3 month follow-up, BDI and DISH assessments were repeated. Patients were characterized as either stable non-depressed, stable depressed, or as a remitter. Only 15 patients became newly depressed and were not included in further statistical analyses. Using clinical data obtained at the time of admission and through chart review, we calculated the GRACE risk-adjustment index to determine the patients' predicted six-month all-cause mortality from the time of hospital discharge. A GRACE score of 80 predicts a 1% mortality at six months, 100 predicts a 2% mortality, and >210 predicts a $>50\%$ mortality. We utilized ANOVA to compare GRACE index scores according to depression status.

Results: The mean age was 61 years (range 25–93), 41% were female, 11% were Hispanic, and 13% were Black. Patients with BDI ≥ 10 at admission had an average GRACE score of 92 (range 25–196), compared to 92 (range 32–187) for those with a BDI 0–4 ($p=0.90$). Similarly, patients who met DISH criteria for depression had no statistically significant difference in GRACE scores versus those who did not; 88 vs. 93 ($p=0.15$), respectively. At 3 months, the patients' depression status contin-

ued to show no statistical association with mean GRACE scores from admission. Using BDI classifications, averages were: stable non-depressed 91, stable depressed 86, remitter 91 ($p=0.28$). Using DISH classifications: stable non-depressed 92, stable depressed 87, remitter 89 ($p=0.49$).

Conclusions: Depressive status after hospitalization for ACS was not significantly associated with the GRACE score, a well-validated measure of cardiac risk severity. If higher mortality is found in the depressed patient group, our finding would strengthen the assertion that depression is an independent risk factor for mortality and that biobehavioral mechanisms such as poor adherence or neurohormonal mediators are causal links.

Impaired Beneficial Effects of Deep Inspiration in Obesity. M. Nudelman¹, S. Liautaud¹, A. Togiash², H. Shaikh¹, A. Chiarelli¹, C. Schechter³ and G. Skloot¹. ¹Mount Sinai School of Medicine, New York, NY; ²Johns Hopkins University, Baltimore, MD and ³Albert Einstein College of Medicine, New York, NY.

Rationale: Airway responsiveness (AR) may be increased in obesity. Low tidal volumes in the obese (O) could increase AR by inhibiting the beneficial effects of deep inspiration (DI). We hypothesized that if this were true, O and nonobese (N) subjects should respond differently to routine (R - with DIs) but not to modified (M - no DIs) methacholine (Mch) challenge.

Methods: R and M challenges were performed in 8 O ($BMI \geq 30$) and 8 N ($BMI \leq 25$) nonasthmatics. Lung function included forced oscillation (FO) and spirometry at baseline and post-Mch (maximal efforts only) as well as after each dose step (for spirometry, maximal or partial efforts in R and M Mch challenges respectively). FO measured resistance at 5 Hz (R5) (global airways index), 20 Hz (R20) (large airways index), and 2 indices of small airways function, R5-R20 and the integrated area of low frequency reactance (AX) (all in $cm^2 H_2O/L/sec$). Post-Mch % change from baseline was calculated.

Results (Mean \pm SE): Baseline lung function revealed significant differences in O vs. N subjects only in FEV_1/FVC (0.80 ± 0.008 vs. 0.86 ± 0.011 , $p=0.002$) and in R5 (3.74 ± 0.16 vs. 2.92 ± 0.21 , $p=0.008$). The mean highest dose of Mch given did not differ between the groups in either challenge. As expected, greater changes were induced by M vs. R challenge in both groups (based on spirometry). The % increase from baseline in small airways indices in the R challenge was greater in O subjects (R5-R20: 43 ± 14 vs. 5 ± 7 , $p=0.02$; AX: 634 ± 199 vs. 88 ± 25 , $p=0.02$) but no significant differences were found in the M protocol (R5-R20: 46 ± 7 vs. 47 ± 13 , $p=0.9$; AX: 836 ± 190 vs. 910 ± 232 , $p=0.8$).

Conclusions: Our results suggest that increased AR in obesity is due to impaired beneficial effects of DI and may be predominantly a small airways phenomenon.

Prognosis of Macrovascular Invasive Hepatocellular Cancer. T. Shao. Mount Sinai School of Medicine, New York, NY.

Background: Therapeutic options are limited for hepatocellular cancer (HCC) patients whose tumors invade major blood vessels. Surgical or locoregional therapies are often not feasible. Survival, infrequently reported has been < 4 months (m) in most series. We sought to better define outcomes and prognostic variables in unresectable macrovascular invasive (MVI) HCC.

Methods: We performed a retrospective analysis of patients evaluated at a medical oncology practice at a liver center during a 5-year period. Records of patients with HCC and tumor invading portal veins (main or branches), hepatic veins or inferior vena cava (IVC) were evaluated with respect to prognostic variables, therapy and overall survival (OS). We included patients who had MVI HCC at diagnosis or at recurrence following initial therapy. Patients with MVI HCC who underwent hepatic resection were not included in this analysis and will be reported elsewhere.

Results: Sixty-one MVI HCC patients were identified who met criteria. Ten had recurrence following prior resection, RFA or embolization; 51 (84%) had MVI HCC at diagnosis. Median age was 62 (range 27-82); 89% were male. Etiology was as follows: HCV 48%; HBV 16%; HCV/HBV 3%; alcohol 16%; PSC 2%; idiopathic 13%. Median OS was 3.2 m; 6-month OS was 23% and 1-year OS was 6%. Univariate analysis indicated that Child-Pugh class, ECOG PS and Barcelona and CLIP scores were strongly associated with OS. Tumor size and type of vascular invasion (branch vs. main vs. IVC) were not associated with differences in OS. A trend towards improved OS was noted in patients age > 60 (4.1 vs. 2.4 m; $p=0.14$) and in patients receiving hepatic artery-based therapy (embolization or chemotherapy) (4.5 vs. 3.1 m; $p=0.06$); patients receiving therapy had similar Child and CLIP scores, but better PS than those not receiving treatment.

Conclusions: MVI HCC is associated with grave prognosis and several of the major classification systems further accurately define prognosis. Additional multivariate analysis will help define the contribution of hepatic artery-based therapy.

Revising the ACR Criteria for Systemic Lupus Erythematosus. V. Singh. Mount Sinai School of Medicine, New York, NY.

Purpose: The Systemic Lupus International Collaborating Clinics (SLICC) has undertaken an effort to revise and update the current ACR classification criteria for systemic lupus erythematosus (SLE).

Methods: Seventy patients were recruited. They were categorized based on the diagnosis given to them at the enrollment site: 56 SLE; 2 undifferentiated connective tissue disease (UCTD); 5 RA, 1 Primary APS; 3 Secondary APS; 4 vasculitis; and 2 dermatomyositis. Case report forms captured clinical and serological features. Serum and plasma were collected and stored for each patient. Patient summaries based on the data from the case report forms were sent to the members of SLICC. 13 SLICC members entered their own diagnosis for each summary, and were asked to do so without regard to the number of ACR criteria. The agreement between SLICC members in their diagnosis for each patient was then assessed.

Results: Considering all the primary ratings, 656 (67%) were SLE, 312 (32%) were non-SLE, and 12 (1%) were uncertain. The Table summarizes the degree of agreement between the raters, overall, and as a function of whether the case satisfied 4 or more ACR criteria for SLE. Perfect consensus was reached for 33 (47%) of the patients. This exceeds the degree of consensus expected by chance ($p < 0.0001$). Of the 27 cases with disagreement, 18 (67%) were due to a disagreement regarding whether the case was SLE or UCTD. The raters varied in the frequency of diagnosis of UCTD from 2 (3%) to 17 (24%). Among those patients with 4+ ACR criteria, perfect consensus was achieved in 24/47 (51%). The Kappa for this degree of consensus is 41%. Among those diagnosed with SLE but with less than 4 ACR criteria, perfect consensus was achieved in 9/23 (39%). The Kappa for this degree of consensus is 38%. The difference in consensus rate between the two groups is not significant ($p=0.35$).

Conclusion: Surprisingly, among experts in SLE, agreement is only fair in diagnosing patients as SLE who have 4 ACR criteria. There is no difference if there are 4 or 3 ACR criteria. The overlap in diagnosis between SLE and UCTD is large. Although 4 ACR criteria are used to classify patients as having SLE for clinical research purposes, it is obvious that this is not the standard adhered to by SLE experts in the diagnosis of SLE. The eventual goal is to develop criteria that would be both reliable and valid in the diagnosis or classification of SLE.

Real-Time Evidence-Based Medicine: An RCT of a Searching Tutorial. R. Stark. Mount Sinai School of Medicine, New York, NY.

Statement of Problem or Question: To practice Evidence-Based Medicine (EBM) in real-time, physicians must quickly retrieve evidence to inform their management decisions. Internal Medicine (IM) residents receive little formal education in electronic database searching, and have identified poor searching skills as a barrier to their evidence-based practice.

Objectives of Program/Intervention: (1) To teach IM residents to ask focused clinical questions about the care of hospitalized patients; (2) to increase IM residents' efficiency in searching PubMed and filtered EBM resources; and (3) to improve IM residents' comfort in searching for primary evidence to guide real-time patient care.

Description of Program/Intervention: The EBM Searching Tutorial was integrated into the inpatient ward rotation for IM residents at Mount Sinai Hospital in New York City. All PGY2 and PGY3 ($n=88$) residents were randomized to either participate in the searching tutorial or to attend control conferences unrelated to EBM. Residents randomized to the searching tutorial ($n=44$) meet in groups of 3-6 for one hour weekly for 4-8 weeks during the academic year. Each session is supervised jointly by a librarian and 1-3 faculty members from the Division of General Internal Medicine. During the sessions, each resident generates a clinical question about an active patient on the service, focusing on issues of diagnosis, prognosis or treatment. Using 3 computers in the room, participants then search the literature to answer their questions. Faculty directly supervise all searches, guiding strategies for searching PubMed and emphasizing the use of ACP Journal Club and the Cochrane database when appropriate. In the last 5 minutes of the conference, participants orally present their search strategy and the evidence that resulted from their search. Evaluation of the searching tutorial is two-fold. All 88 residents will complete self-assessment surveys before and after participating in the searching or control conference. The survey was developed by the SGIM EBM Task Force and

measures EBM searching skills and comfort. In addition, searching skills will be measured with an objective structured clinical evaluation (OSCE). Participants will be asked to search for primary evidence to answer a series of clinical questions. Their ability to quickly find quality evidence, appropriate use of filtered resources, and searching techniques will be measured. Investigators scoring the OSCEs will be blinded to group allocation.

Findings to Date: We have surveyed 78 (89%) IM residents prior to the intervention. When provided with a clinical scenario, 95% and 96% report they would utilize PubMed or UpToDate®, respectively, to answer their question. More residents would consult with a peer (64%) or a specialist (50%) than use filtered resources such as Cochrane (26%) or ACP Journal Club (28%). Despite reporting high use of PubMed, only 35% of respondents report feeling very comfortable using it. Few residents report being very comfortable using Cochrane (6.7%) or ACP Journal Club (2.7%). Post-intervention surveys and OSCE evaluations are ongoing.

Key Lessons Learned: IM residents frequently use online textbooks (UpToDate®) and PubMed to answer clinical questions, but rarely use filtered resources. Their self-reported comfort with PubMed and filtered resources is low. We hypothesize that real-time teaching of searching skills in the context of patient care will improve these skills and promote evidence-based practice.

Limitation of the Resting Ankle-Brachial Index in Symptomatic Patients with Peripheral Arterial Disease. R. Stein, I. Hriljac, J.L. Halperin, S.M. Gustavson, V. Teodorescu, and J.W. Olin. Mount Sinai School of Medicine, New York, NY.

Abstract: Peripheral arterial disease (PAD) has been demonstrated to be prevalent in the primary care setting. However, it has also been shown to be unrecognized and under-treated. Owing to the association with cardiovascular disease it has been recommended to screen high-risk patients for PAD in the primary care setting using the ankle-brachial index (ABI). ABI has been demonstrated to be highly sensitive and specific in diagnosing PAD in patients with significant stenosis. However, the utility in patients with less severe stenosis and calcified vessels is in question. The aims of this study were to determine the diagnostic utility of measuring the ABI at rest in patients referred to the vascular laboratory for evaluation of suspected PAD, and to assess the added value of pulse volume recordings and post-exercise studies in patients with a normal ABI. A computerized vascular diagnostic laboratory database was queried for symptomatic outpatients referred for measurement of segmental blood pressure, the ABI or pulse volume recordings by physicians not specialized in the evaluation and management of patients with peripheral vascular disease. Of 707 patients undergoing outpatient physiologic arterial evaluations between February 1, 2003 and July 31, 2004, 396 met these inclusion criteria. Data recorded included resting ABI, ABI following treadmill exercise test and the presence of abnormal pulse volume recordings. The study population (n = 396) consisted of equal numbers of men and women (mean age 69 years, range 19–100 years). Among 396 studies, resting ABI values were normal in 183 (46.2%) and abnormal in 159 (40.2%). Of the 138 patients who underwent exercise testing, 84 had normal ABI readings at rest. In the 84 patients who had a normal ABI at rest and underwent exercise testing, the ABI fell below 0.9 after exercise in 26 (31%). Arterial non-compressibility was detected in 54 (13.6%) patients, whose average age was 67 years. Thirteen (24%) of those with non-compressible vessels had abnormal pulse volume recording (PVR) results, compared to five with normal resting ABI who had abnormal PVR findings (2.7%). In conclusion, this study demonstrated that nearly half of patients referred to the outpatient vascular laboratory because of suspected arterial disease had a normal resting ABI. While it is recommended that the ABI be measured at rest in patients at risk of PAD in primary care practice, these findings suggest that patients with symptoms of PAD should be more completely evaluated in a vascular laboratory. Furthermore, when the ABI is normal at rest in patients with symptoms of intermittent claudication, exercise testing is recommended to enhance the sensitivity for detection of PAD.

“Single-Bite” versus “Double-Bite” Biopsy Specimens: Is There a Difference? J.E. Stern, D.A. Greenwald, E. Ochoa, L. J. Brandt, B. Pothuri, and D. Gelrud. Mount Sinai School of Medicine, New York, NY.

Background: Many gastroenterologists currently take endoscopic biopsies using the double-bite technique, in which two biopsy specimens are obtained during a single pass of the forceps. We hypothesized that the overall quality of biopsy specimens from the double-bite technique is inferior compared to specimens obtained from a single-bite technique.

Methods: The study was prospective and partially blinded. Endoscopic biopsies were taken using each technique. The double-bite tech-

nique involved taking an initial biopsy, repositioning the forceps, and taking another biopsy from the same area with the initial specimen still on the forceps. The single-bite technique involved removing the forceps with its specimen after a single bite. At each site, 4 specimens were obtained, 2 using the double-bite and 2 using the single-bite technique. The specimens were then sent to a single, blinded pathologist. The specimens were evaluated for: diameter (whether the sample was > 2 mm), depth (whether muscularis mucosa was present), percentage of specimens crushed, percentage of specimens torn or sheared, percentage of specimens that did not contain superficial epithelium, and overall diagnostic quality of the specimen (graded: 1=good, 2=moderate, 3=poor).

Results: Of the 29 patients enrolled in the study, 18 patients underwent EGD and 11 underwent colonoscopy. 74 biopsies were taken with each method. The pathologist received 71 of the 74 single-bite (96%) and 63 of the 74 (85%) double-bite specimens (p=0.025). 69 single-bite (97%) and 59 double-bite (94%) specimens had a diameter over 2 mm (p=1.0). 42 single-bite (59%) and 38 double-bite (60%) specimens had muscularis mucosa (p=1.0). 16 single-bite (23%) and 12 double-bite (19%) specimens were crushed (p=1.0). 50 single-bite (70%) and 42 double-bite (67%) specimens were torn (p=0.1). 35 single-bite (49%) and 33 double-bite (52%) specimens had no superficial epithelium (p=1.0). Of the single-bite specimens, 68 had an overall diagnostic quality grade of good, 2 had a grade of moderate, and 1 had a grade of poor. Of the double-bite specimens, 62 had a grade of good and 1 had a grade of moderate.

Conclusion: There is no difference in the overall diagnostic quality of biopsy specimens obtained from either the single-bite or double-bite technique. However, there are a statistically significant number of specimens lost from the double-bite technique when compared to the single-bite technique.

Discontinuation of Standing Opioid Orders for Individuals Transferred from Nursing Home to Hospital. M. Suchanek, K.S. Boockvar, T.R. Fried, and R.S. Morrison. Mount Sinai School of Medicine, New York, NY.

Objectives: Patients in nursing homes commonly experience pain requiring continuous and potent analgesia; however, continuity of care for these patients is often interrupted by admission to the hospital. The objective of this study was to examine continuity of opioid prescribing when individuals are transferred from nursing home to hospital and to examine predictors and consequences of opioid discontinuation.

Methods: Participants were residents of six nursing homes (1 VA) admitted to three hospitals (1 VA) in the New York City metropolitan area between 1999–2004. Nursing home and hospital records were reviewed to identify medication regimens just before and after transfer between sites. Medications were matched and compared in dosage, route and frequency of administration. Associations between opioid use and patient demographics, physical function, comorbidity, APACHE illness severity, care setting (VA or non-VA), and hospital length of stay were examined in bivariate and multivariate analyses. A structured review of selected medical records was performed to ascertain the impact of opioid prescribing decisions between facilities.

Results: A total of 315 nursing home residents experienced 498 hospital admissions. On average patients were 81 years old; 57% were female, 52% white, 30% black, 12% Hispanic, and 50% demented. Patients were taking a routine opioid analgesic just prior to 72 (14%) hospital admissions. In 33 (46%) instances, routine opioid analgesia was discontinued upon hospital admission. After adjusting for demographic and clinical differences, patients in the VA setting were more likely to be taking an opioid analgesic prior to hospital admission (OR 2.58; 95%CI 1.04–6.44). No demographic or clinical characteristic was associated with opioid discontinuation. After controlling for illness severity and other clinical and demographic characteristics, opioid discontinuation was not associated with hospital length of stay. Additional results of structured review of selected medical records demonstrated incidences of patient withdrawal symptoms as well as sub-optimal pain control after interruption of opioid use.

Conclusions: Opioid discontinuation is common practice for individuals transferred from nursing home to hospital and is especially relevant in the VA setting. Further research is necessary to determine the appropriateness of opioid discontinuation and to investigate whether it is associated with patient outcomes such as pain, delirium, and withdrawal symptoms.

Impact: Improving continuity of opioid prescribing for patients transferred between sites of care could prevent iatrogenic harm.

Resections of Benign Hepatic Tumors. P.K. Sun¹, P. Martin¹, M.I. Fiel², S. Roayaie², P. Lopez¹, and M.D. Schwartz². Departments of ¹Medicine, ²Pathology, and ³Surgery, Mount Sinai Medical Center, New York, NY.

Abstract: Benign hepatic tumors remain an important indication for hepatic resection. We review our experience of hepatic resections over a 15-year period at Mount Sinai Hospital, a major referral center for liver diseases located in New York City, to determine how the major indications for resection have changed and whether benign tumors are now a less frequent indication of hepatic resection. The service has performed over 250 resections of benign hepatic tumors since 1990. Through retrospective analysis of patient records, we examined: (1) the diagnoses of benign hepatic tumors resected at a major referral center, (2) the gender and age demographics of each diagnosis seen, and (3) how these factors have changed, if at all, over time. Between January 1990 and December 2004, 236 patients had surgical resection of benign hepatic tumors. The most common indications, in descending order, were hemangioma (n = 90; 38.1% of total subjects), simple cyst (n = 42; 17.8%), focal nodular hyperplasia (FNH) (n = 36; 15.3%), and hepatic adenoma (n = 30; 12.7%). For almost all diagnoses, the majority of patients were female (83.9% of all patients). Among common indications, FNH and simple cyst were associated with the highest percentage of female patients (FNH—94.4% females, 5.6% males; simple cyst—88.1% females, 11.9% males). Several less common diagnoses also had a marked female predominance: biliary cystadenoma, nodular regenerative hyperplasia, and angiomyolipoma were seen exclusively in female patients, and polycystic liver disease (92.3% females, 7.7% males) was seen almost exclusively in female patients. The mean age of all subjects was 48.1 years. Patients with FNH and hepatic adenoma had the youngest mean ages (36.5 and 38.2 years, respectively) among all diagnoses. The oldest mean ages were seen with inflammatory pseudotumor (62.0 years) and simple cyst (60.4 years). 39.2% percent of patients with laboratory data available had hepatobiliary abnormalities, most commonly mild elevations of alkaline phosphatase, transaminases, or total bilirubin. Benign hepatic resections comprised 22.8% of all hepatic resections over the 15-year study period. There were no clear temporal trends over the study period in the proportion of individual diagnoses, gender, or age, or the number of benign hepatic resections as a percentage of all hepatic resections.

Assessment of an HIV Educational Program in Ethiopia. M. Swaminathan and R. Hodes. Mount Sinai School of Medicine, New York, NY.

Background: HIV infection is a growing problem in Ethiopia. Educational programs have been implemented to reduce high-risk sexual practices and prevent the transmission of HIV but few studies have been conducted to test their effectiveness.

Methods: A total of 205 surveys were distributed amongst the clinic population of an NGO, which provides educational information as well as contraception. The survey assessed the attitudes and knowledge of HIV as well as towards safe sexual practices of the population. The population was also surveyed to determine their current sexual practices as well as their use of contraception.

Results: 58.4% of the population used some form of contraception in the previous year. Of these 12.4% used oral contraceptives, 50.5% used hormonal injections, and 1.0% used surgical sterilization. None used condoms or other forms of barrier contraception. 5.4% admitted to having sexual relations with more than one person in the previous year, 3.9% with someone they only knew casually and 1% admitted to having sexual intercourse with a commercial sex worker. There was much misinformation concerning HIV. Only 71.2% of patients believed condoms were effective in preventing acquisition of HIV, 29.9% believed that mosquitoes were carriers of HIV, 9.4% believed HIV was an airborne infection, and only 16.2% believed that abstinence was an effective protection against acquiring HIV.

Conclusion: High-risk sexual behavior is still prevalent as well as misinformation concerning HIV infection and transmission. Much work needs to be done in determining effective ways to change high-risk behavior beyond current educational and health promotion programs.

Palliative Care in the ICU. V. Veve. Mount Sinai School of Medicine, New York, NY.

Background: More than 60% of the approximately 2.5 million deaths in the US each year occur in hospitals. Almost half of these patients have been cared for in an ICU in the last 3 days prior to death. Hospital care for patients at the end of life is characterized by poorly controlled pain and other symptoms. Palliative care (PC) consultation for ICU patients has

been growing; this is improving patient outcomes such as pain and symptom control, and family outcomes such as quality of care and satisfaction. Palliative care consultation in the ICU, can decrease hospital length of stay LOS and shift goals of care to comfort much earlier in the disease process for patients at high risk of death.

Objective: To describe pilot data on selected quality of ICU care indicators for patients who die in ICU. To examine differences in quality of ICU care for patients who received PC compared to usual care (UC).

Methods: Using the VA National Medical SAS Inpatient Datasets, we identified a cohort of veterans who died in the hospital at the VA between October 1, 2003 and December 31 2005 in ICUs with the length of last hospitalization greater than 48 hours. We developed a chart review tool to collect information on practice patterns in the ICU. The following information was collected: decision making by patient and/or family, evidence of advance directives, documentation of family meeting, evidence that the patient was considered dying, evidence of explicit plan of comfort care, presence of symptoms and symptom management, initiation of therapeutic interventions, discussion of their withdrawal, patient and family preference, whether PC was consulted or not, and death data. We will describe pilot data on selected quality of ICU care indicators for patients who die in ICU and examine differences in quality of ICU care for patients who received palliative care compared to usual care. We will determine the prevalence of selected quality of ICU care indicators for patients who die in ICU and examine with univariate descriptive statistics. We will use logistic regression to examine differences in prevalence of the four quality-of-care indicators for PC compared to UC patients. Control variables include patient age, diagnosis and reason for ICU admission and LOS.

Preliminary Results: Preliminary analysis shows that in FY04, a total of 132 patients died in the VAMC:84 (38.4%) in the ICU and 68 (31.1%) in the acute care wards. PC patients differed significantly from usual care patients in a number of ways. For example, compared with PC patients, UC patients had more comorbid conditions, were more likely to have a principal diagnosis of cardiovascular diseases but less likely to have cancer, and were less likely to be on medical service. Multivariate results are forthcoming.

MMP-2 Regulates Collagen I mRNA Levels in Hepatic Stellate Cells: Potential Mechanism for Protective Role of MMP-2 in Liver Fibrosis. R. Vrabie, R. Gupta, J. Martignetti, M. Ramirez, F. Hong, B. Radbill, and M. B. Bansal. Mount Sinai School of Medicine, New York, NY.

Introduction: Matrix metalloproteinase-2 (MMP-2), a type IV collagenase produced by activated hepatic stellate cells, is increased in patients with chronic hepatitis and cirrhosis, suggesting a causative role in the fibrotic process. The current dogma suggests that MMP-2 is pathologic by accelerating the degradation of the normal basement membrane allowing for replacement by type I collagen, the collagen characteristic of the cirrhotic liver. Our lab has previously demonstrated that MMP-2 serves a protective role as MMP-2^{-/-} mice develop more histologic fibrosis (increased collagen I) in a toxin-induced model of liver injury and this increased fibrosis is not associated with differences in hepatocellular injury or degradation of collagen I but is associated with increased collagen I mRNA levels (n=6; 107% increase, p<0.0001). The mechanism by which MMP-2 regulates collagen I mRNA levels is not known.

Hypothesis: We hypothesize that MMP-2 directly regulates collagen I mRNA levels.

Methods: To determine whether endogenous MMP-2 is present within the nucleus of LX2 cells, a human hepatic stellate cell line, Western blot was performed on 30 µg of nuclear extract and probed for MMP-2. To determine whether MMP-2 is regulating collagen I mRNA levels, LX2 cells were transfected with either WT-MMP-2 or empty vector control. Effects of overexpression of MMP-2 on collagen I mRNA levels were examined by real-time PCR. In addition, to determine whether "MMP-2 knockdown" would have opposite effects on collagen I mRNA levels when compared to effects of MMP-2 overexpression, MMP-2 targeted siRNA (100 nm) or non-targeting siRNA (siControl) was transfected into LX2 cells and collagen I mRNA levels examined by real-time PCR. Transfection of non-targeting siRNA was used as a baseline to control for off-target effects of siRNA in these cells. To determine whether MMP-2 can transactivate the collagen I promoter, LX2 cells were cotransfected with WT-MMP2 or empty control vector along with collagen I promoter-Luciferase deletion constructs (2.2 kb, 1.8 kb, 906 bp, 220 bp, 133 bp, 120 bp, and 92 bp).

Conclusions: Both pro- and active MMP-2 were found within the nucleus of LX2 cells. Overexpression of WT-MMP-2 resulted in a 40% decrease (n=5, p<0.014) in collagen I mRNA levels and conversely there was a 66% increase (n=4, p<0.001) in collagen I mRNA levels in the LX2 cells in which MMP-2 had been "knocked down." These findings suggest a direct link between MMP-2 and collagen I mRNA regulation. Preliminary results of

co-transfection of collagen I promoter-luciferase constructs and WT-MMP-2 suggests a potent repressor element located between 2.2 kb and 1.8 kb of the collagen I promoter. These results point to a novel role of MMP-2 in modulating gene transcription and will be explored in future studies.

Natural History of Dysplasia in Inflammatory Bowel Disease—Is Colonoscopic Surveillance of Dysplastic Lesions in IBD Justified? D. Wild, M. Sparrow, A. Cheifetz, P. Rubin, C. Bodian, and D. Present. Mount Sinai School of Medicine, New York, NY.

Background: There is no doubt that patients with long-standing inflammatory bowel disease (Crohn's Disease [CD], Ulcerative Colitis [UC] and Indeterminate Colitis [IC]) are at increased risk for colorectal cancer (CRC), several large reviews have estimated the incidence ratio to be 2–3 times that seen in the general population (1, 2). It is for this reason that a reason consensus panel advocates initiating a program of colonoscopic surveillance 8–10 years after the diagnosis of IBD is made and continuing every 1–2 years in attempt to achieve early detection of pre-malignant or dysplastic lesions (3). Once these dysplastic lesions are detected, there is a considerable amount of controversy surrounding how best to manage these patients. Studies have found the risk of low grade dysplasia (LGD) progressing to high grade dysplasia (HGD) or frank carcinoma ranges from 10–53% leading many specialists to advocate an aggressive approach that favors early surgical resection of colons in which any form of dysplasia has been detected (4, 5). An aggressive surgical approach is associated with a considerable amount of physical and psychological sequelae leading many patients and their practitioners to utilize a more conservative approach with frequent, careful colonoscopic surveillance, turning to surgery only after LGD is found on multiple serial exams or a lesion with HGD is detected. We performed a retrospective review of the charts of a single, experienced IBD specialist in an attempt to show that a careful conservative strategy could be utilized without significantly increasing the incidence or CRC or rates of death from it.

Methods: Utilizing colonoscopy result log books, we identified patients with IBD who at some point developed LGD, HGD or indeterminate dysplasia in either flat or polypoid mucosa as diagnosed by an experienced pathologist between roughly 1970 and 2005. We then retrospectively reviewed the patients' charts, recording all previous and subsequent colonoscopy and pathology results.

Results: While this study is still in the data analysis stage and so the final data is still pending, preliminarily we can say the following: we identified a cohort of 140 patients with IBD (87 with UC, 45 with CD and 8 with IC) who at some point had a dysplastic lesion. Eleven cases of CRC developed in the patients with UC, 5 cases of CRC were found in the patients with CD and 1 case was found in the patients with IC. The majority of cases of CRC were detected in an early stage that was entirely curable by resection.

Conclusion: No conclusions can be drawn until the data have been completely analyzed.

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Effect of Depression and Four Commonly Prescribed Anti-depressants on the Platelet Reactivity of Coronary Artery Disease Patients. M.U. Zafar, K. Hiensch, G. Vilahur, B. Ibanez, K. Davidson, J. Gorman, V. Fuster, and J. Badimon. Mount Sinai School of Medicine, New York, NY

Background: Depression is a frequently observed co-morbidity in coronary artery disease (CAD) patients following an acute coronary event. Conversely, depression in CAD patients has been linked to a higher incidence of recurrent coronary events. Although the mechanism of this relationship is not fully understood, it is presumably due to a higher serotonin-mediated platelet-reactivity in depressed CAD patients. There is some evidence suggesting that anti-depressive therapy can be helpful in reducing

coronary events, but whether the mechanism is central or a direct effect on platelets remains unclear. We compared platelet reactivity in depressed vs. non-depressed CAD patients and assessed the effect of 4 commonly prescribed antidepressants on platelets.

Methods: Stable CAD patients with (n=13) and without (n=15) depression were enrolled. Depression was assessed using the Beck Depression Inventory using a cutoff score of ≥ 10 . Patients on anti-depressive therapy were excluded. Platelet reactivity was assessed by optical aggregometry in response to adenosine diphosphate (ADP) (5 μ M) and serotonin (10 μ M). In order to assess the direct effect of the anti-depressive drugs (nefazodone, duloxetine, escitalopram and sertraline) on platelet reactivity, each drug was mixed *in vitro* with the patient's blood in separate tubes. Concentrations of the drugs were calculated to match plasma levels achieved with commonly prescribed clinical doses (nefazodone 200 mg/day, duloxetine 60 mg/day, escitalopram 10 mg/day and sertraline 100 mg/day). To serve as a comparative control, one tube of blood was mixed with equal volume of normal saline.

Results: Depressed CAD patients had higher platelet reactivity vs non-depressed CAD patients. Except for nefazodone, each drug significantly reduced serotonin-mediated platelet aggregation, with sertraline being the most potent. No effect on ADP mediated aggregation was seen.

Conclusions: Depressed CAD patients have increased platelet reactivity which plays an important role in the higher coronary event rate seen in this population. The effect on platelet reactivity exerted by the 4 anti-depressive drugs in our study was not the same. Sertraline appeared to have the most potent anti-platelet effect while nefazodone appeared to be the weakest. Our data strongly emphasizes the importance of selecting the proper anti-depressive therapy, particularly in CAD patients, if the dual benefit of improving depressive symptomatology and inhibiting platelet reactivity is to be obtained.

Antithrombotic Effects of Direct Factor-Xa Inhibition: A New Therapeutic Modality. M.U. Zafar, D. Vorchheimer, B. Choi, G. Vilahur, B. Ibanez, P. Moreno, V. Fuster, and J. Badimon. Mount Sinai School of Medicine, New York, NY.

Background: Cardiovascular disease remains the leading cause of death in the United States. Although potent therapeutic options are available, there is an ever-present need to discover newer, more novel methods to address this problem. Tissue factor pathway inhibition is a new therapeutic target in the treatment of atherothrombotic disease. Standard indirect factor Xa (FXa) inhibitors (i.e., heparin and warfarin) have proven to be effective but require cumbersome monitoring due to their bleeding complications. Injectable direct FXa inhibitors offer better safety, with efficacy comparable to current treatments. These benefits could be extended to the ambulatory setting with an oral agent. We evaluate the antithrombotic effects of an oral direct FXa inhibitor DU-176b in a phase I human study.

Methods: Healthy subjects (n=12, males=8, 28 \pm 6 years) received a single, 60mg dose of DU-176b. Antithrombotic effects of FXa inhibition were assessed by changes in thrombus size pre- and post-treatment, using the Badimon perfusion chamber. The chamber allows *ex vivo* perfusion of human blood over pig aorta at venous and moderately stenosed arterial flow conditions, resulting in thrombus formation over the pig aorta. Area of the thrombus is then measured using Image Pro Plus software. Chamber studies and measurements for anti-FXa activity and thrombin generation were performed pre-dose, and at 1.5-, 5- and 12-hours post-dose.

Results: Factor Xa inhibition by DU-176b resulted in a significant reduction in thrombus size and thrombin generation. The antithrombotic effect was rapid in onset, showing maximum effect after only 1.5 hours of dosing, and remained significant even at 5 hours. At 12 hours post-dose, the thrombus size was back to pre-treatment levels. Changes in thrombus size and thrombin generation closely followed the changes observed in the clotting parameters.

Conclusion: Factor Xa inhibition by DU-176b, a novel, oral, direct FXa inhibitor, significantly reduced thrombus formation (venous and arterial) and thrombin generation upto 5 hours post-dose. The antithrombotic effect mirrored changes in the clotting parameters, which could be used for monitoring in a clinical setting. The implications of Tissue factor pathway inhibition by DU-176b as a new therapeutic tool requires further study in larger clinical trials.

A Novel Nitric Oxide Donor (LA-419) Has Anti-thrombotic Properties in a Human Model of Thrombosis. M.U. Zafar, G. Vilahur, B. Choi, B. Ibanez, E. Salas, V. Fuster, and J. Badimon. Mount Sinai School of Medicine, New York, NY.

Background: Healthy endothelium exerts its protective antithrombotic effect via nitric oxide (NO) synthesis. NO is one of the most potent anti-platelet agents. Nitrates are known to have anti-platelet effect but only at supra-therapeutic doses. A NO donor exerting its effect primarily on

platelets could offer the benefit of anti-platelet properties without prohibitive vasodilation. We studied the antithrombotic effect of a novel NO donor LA-419, with known anti-ischemic properties but no vasoactive effects.

Methods: Healthy males (n=8) received aspirin (325 mg/day) for 3 days prior to participating in 3 consecutive study arms; (a) LA-419 (10 mcg/mL) and (b) LA-419 (20 mcg/mL) and (c) abciximab (4 mcg/mL), serving as positive control. Non-anticoagulated blood was perfused through the Badimon chamber for anti-thrombotic assessments pre- and post-treatment, at venous and arterial flow rates.

Results: There was a dose-dependent decrease in thrombus formation at both venous and arterial flow conditions with LA-419. Abciximab was a very potent inhibitor of thrombus growth, as expected.

Conclusions: LA-419, a novel NO-donor, shows a dose-dependent antithrombotic effect, evidenced by a significant reduction in thrombus formation from baseline values, at both venous and arterial flow conditions. Our observations suggest that the availability of a NO-donor could prove beneficial in the prevention of thrombotic complications of cardiovascular disease and requires further clinical studies.

Left Atrial Size Can Identify the Highest Risk Multicenter Automatic Defibrillator Implantation Trial-II Patients for Ventricular Arrhythmic Events. A. Zohlman, L.B. Croft, D. Mehta, and M.E. Goldman. Mount Sinai School of Medicine, New York, NY.

Background: In the Multicenter Automatic Defibrillator Implantation Trial (MADIT)-II, implantable defibrillators (ICD) reduced mortality from 19.8% to 14.2% in patients with reduced left ventricular (LV) function and coronary artery disease over 20 months. However, in the control group, >80% of patients survived. Variables including QRS width, New York Heart Association class, LV ejection fraction (EF) or age were not predictive of survival. With 400,000 new eligible patients annually, the cost of ICD's would overwhelm the health care budget. Left atrial volume has been identified as a predictor of morbidity and mortality. Therefore we sought to evaluate whether left atrial area (LAA) or other echocardiographic (echo) parameters could identify the highest risk MADIT-II patients.

Methods: We retrospectively reviewed all patients over the last eight years that had an implantable cardiac defibrillator (ICD) placed from 1997–2005 and had an echocardiogram (echo) within a year of implantation. LAA, LV EF, 2-D LV size, wall stress, and ventricular events (episodes of ventricular fibrillation and/or ventricular tachycardia) requiring shock as documented by their ICDs were analyzed.

Results: Of 156 patients with ICD implanted and a recent echo, 60% met MADIT-II criteria. There was no difference in age, QRS width, LV EF, blood pressure or wall stress between patients with ventricular events and non-event patients. However, LAA (30 cm² vs. 25 cm², p=0.0004) was greater in those with at least one ventricular event.

Conclusion: LAA was a strong correlate of ventricular events which and potentially better identify the highest risk MADIT-II ICD eligible patients.

Jersey City Medical Center

Contrast Induced Neurotoxicity in a Patient with Normal Pressure Hydrocephalus. K. Patel, M. Ratanu, A. Andrade, and J. Matta. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

Introduction: Contrast induced neurotoxicity is a rare but serious complication of coronary angiography. Non-ionic contrast media (CM) markedly decreases neurotoxic complications. Non-ion CM has been reported to cause transient cortical blindness, confusion and amnesia but no focal deficits, whereas ionic CM is associated with seizures, and motor and speech deficits. We report a patient who developed focal seizure and an acute confusional state after coronary angioplasty.

Case Report: A 65-year-old female with a history of DM presented for nausea and vomiting and ruled in for non-ST elevation myocardial infarction. She underwent transfemoral coronary angioplasty. Coronary angioplasty was done over 120 minutes, using 400 mL visipaque (iodixanol-non ionic CM). There were no complications during the procedure. After 30 minutes, patient was found very confused with some twitching movement of tongue and right upper limb. CT head was done within 2 hours, which showed subarachnoid hemorrhage vs. meningitis. Within 36–40 hrs, the patient's mental status was improved significantly but she continued having nausea and dizziness. Repeat CT head next day still showed findings suggestive of subarachnoid hemorrhage. Third CT head showed contrast material stasis in the leptomeningeal vessels rather than subarachnoid hemorrhage. There was also evidence of communicating hydrocephalus. Retrospectively, patient's family claimed that patient had

prior symptoms consistent with normal pressure hydrocephalus. Lumbar puncture was performed which showed protein 67 and normal opening pressure without any evidence of infection.

Discussion: We report on a patient who developed focal seizures and acute confusional state after coronary angioplasty. CM can cause neurotoxicity secondary to osmosis or embolism. We hypothesize that the symptoms here were due to direct toxic effect of contrast media, which in our patient stayed in contact with cerebral cortex for prolonged period of time secondary to the presence of normal pressure hydrocephalus.

Seizure Induced Neurogenic Pulmonary Edema. S. Hosadurga, K. Patel, M. Ratanu, A. Andrade, and J. Matta. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

Introduction: Neurogenic pulmonary edema (NPE) characteristically presents within minutes to hours of a severe central nervous system insult. We report a patient who developed NPE after an episode of seizure.

Case Report: A 47-year-old African-American female with a history of hypertension and seizure disorder noncompliant to medication was admitted for witnessed tonic clonic seizures. Patient was found confused and short of breath after the seizure. Patient quickly desaturated to 88%. Physical examination revealed tachypnea, tachycardia and bibasilar rales that were consistent with pulmonary edema. Chest X-ray showed bilateral pulmonary edema. Stat CT scan showed diffuse infiltration consistent with pulmonary edema. Echo was normal. Patient's oxygen saturation improved with oxygen supplementation and seizures were controlled on Trileptal. Next day patient's mental function and oxygen saturation improved. Repeat CT scan of chest within 24 hours failed to show any pulmonary edema. The diagnosis of NPE was made.

Discussion: The pathogenesis of NPE is not completely understood. Because the most common neurological events are associated with increased intracranial pressure, intracranial hypertension is considered a key factor. The results in stimulating the hypothalamus and vasomotor centers of medulla oblongata which leads to activation of the sympathetic system and increased pulmonary capillary permeability. The outcome of patients with NPE depends on the initial neurological insult. NPE managed in a supportive and conservative fashion and usually resolves within 48–72 hours.

Clinical Suspicion Aids in Treatment of Toxic Ingestion Outcome. A. Kimel, C. Tadros, and D. Flores. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

A 54-year-old male was found by his family after stumbling, falling to the ground. He presented with confusion, blurry vision and elevated blood pressure. The patient had past history of severe depression. He denied any history of alcohol or any illegal drug use. ICU evaluation was called immediately as patient's mental status was deteriorating and became lethargic with respiratory rate of 8. He was intubated for airway protection and stabilization. On initial physical exam he was found to have slowly reactive pupils, not nystagmus, no oral-pharyngeal lesions, increased tone of the bilateral upper extremities and a decreased gag reflex. On breath exam there was a hint of a sweet odor. Patient was started empirically on antibiotics and aggressive hydration. Laboratory results revealed a sodium level of 138 (meq/L), potassium of 4.1, chloride of 111, bicarbonate of 9, BUN of 7, Cr of 112 and glucose of 112. Calcium was 9.0, magnesium was 2.2 and phosphorus of 2.7. An arterial blood gas analysis indicated severe metabolic acidosis. The anion gap was 1u with a calculated osmolar gap of 122. We began treatment for acute ethylene glycol poisoning based on high clinical suspicion. Fomepizole was administered at a dose of 15/mg/kg IV. Subsequently, the patient's creatinine increased 1.0 to 3.5mg/dL.

The patient became completely anuric within 30 hours of arrival. After failure of aggressive hydration, hemodialysis was instituted. Urine analysis revealed a urine oxalate level of 125 (units) and many calcium oxalate crystals. The family returned with an opened container of antifreeze found in the garage, but did not own an automobile. Our patient was extubated and did admit to a suicide attempt. The patient continued on hemodialysis for over one year due to severe renal impairment.

Discussion: Early in ethylene glycol intoxication the sole compound of ethylene glycol is present. As time passes, toxic metabolites accumulate and the patient develops metabolic acidosis. Eventually, oxalate is deposited in the kidney and elsewhere; renal insufficiency can occur. Once any of these manifestations occurs, antidotal therapy alone (used to block alcohol dehydrogenase with fomepizole or ethanol) is sufficient to treat the poisoning. In the presence of high clinical suspicion and laboratory data consistent with acute ethylene glycol ingestion, early administration

of fomepizole is critical to avoid long-term sequella of renal failure in such intoxications.

IgA Nephropathy: Progression of Segmental Glomerulosclerosis and Crescent Formation after Complicated Pregnancy. T.S. Borisiak, K. Khan, E. Martinez and B. Weiner. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

Case: A 32-year-old Pakistani female with no medical history of kidney disease or complaints, developed face and leg swelling and dark urine following 8 weeks s/p complicated pregnancy. In the second trimester she developed hypertension and in third became pre-eclamptic and was rushed into delivery via c-section at 36 weeks' gestation. As per medical records her renal function was within normal limits and urinalysis revealed slight proteinuria only in third trimester. She offered no complaints postpartum till present time. Labs on admission: Hgb, 11.3; Pl5, 454; BUN, 4; Alb, 1.1. LFT, within normal limits; hepatitis profile—negative; urinalysis 500 protein, >10 RBC, no casts; neg. serology for SLE and C3, C4 complement levels are within normal range. The 24-hour urine collection revealed massive proteinuria (15g/d). Renal sonogram was unremarkable. Renal biopsy was done. Pathology: IgA nephropathy, diffuse segmental endocapillary and sclerosis glomerulonephritis with crescent formation. Patient was discharged home on ACE inhibitors and furosemide for symptomatic relief.

Discussion: IgA nephropathy is a chronic progressive glomerular disease with infrequent reversal. Crescentic glomerulonephritis is a rare presentation of IgA nephropathy and associated with more rapidly progressive renal failure and poor prognosis. The increased renal blood flow and hyperfiltration that occur during pregnancy may potentially aggravate the sclerosing process.

Conclusion: Pregnancy could play an important role in worsening previously asymptomatic kidney disease.

Halitosis Heraldng Pyogenic Liver Abscess. N. Javier, A. Obiefuna, C. Ukpong, and P. Bhatt. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

Introduction: The liver is the most commonly involved organ in a visceral abscess. The two major mechanisms are local spread from contiguous infections with the biliary tree or peritoneal activity, and hematogenous seeding. The latter is not the usual pathway.

Case: A 45-year-old male with hypertension, depression and mild mental retardation presented with a one-day history of right upper quadrant abdominal pain and fever. He had acute leukocytosis and hyperbilirubinemia. Initial impression was of acute abdomen. Ultrasonography showed a hypochoic hepatic mass. Computed tomography (CT) indicated acute cholecystitis vs. pancreatitis. The HIDA scan was normal. Chest X-ray was significant for right-sided inferior lung field infiltrate. A diagnosis of pneumonia with right-sided pleural base reaction was made. After starting IV antibiotics, the patient felt better despite having intermittent febrile episodes. He was advised completion of a 14-day regimen of oral antibiotic upon discharge. One, week later, the patient was readmitted for similar symptoms. However, the abdominal pain was more pronounced in the epigastrium. Another abdominal CT was done which revealed multiple lesions in the left hepatic lobe and porta hepatis. The patient underwent endoscopy that showed an extrinsic mass compressing the done subsequently. The specimen grew *Streptococcus viridans*. There was partial resolution of the hepatic lesions with dramatic improvement in the patient's symptoms. The amebic titer and tumor was unremarkable. On further history, the patient's mother had observed that her son had significant halitosis several months prior to the onset of symptoms despite daily oral hygiene. He was finally discharged on oral antibiotics and advised repeat CT with colonoscopy with one week.

Discussion: This case illustrates the variability and the non-specificity of the clinical presentation of patients with pyogenic liver abscess. Clinicians should therefore have a high index of suspicion. Hematogenous seeding from transient bacteremia either coming from the oral cavity or a possible underlying malignancy are proposed pathophysiologic mechanisms for the occurrence of a pyogenic liver abscess in an otherwise low risk patient.

The Enigmatic Kikuchi Fujimoto Disease. N. Javier, X. Mduli, S. Kazmi, and R. Chinai. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

Introduction: Kikuchi's disease is a benign, self-limiting clinicopathologic disease with protean and nonspecific symptoms. It occurs worldwide, affecting mostly Asian women.

Case: A 32-year-old male from South India presents with a 3 23k history of intermittent febrile episodes, chills, night sweats, fatigue and myalgia. He had no recent travel, vaccinations, exposure to pets and sick contacts, illicit drug use, sexual promiscuity, and occupational hazards. His initial work-up in the clinic included a negative Mantoux test and a normal chest X-ray. In the hospital, his physical exam was significant for multiple mobile anterior cervical right-sided lymph nodes. His blood tests showed leukopenia (2,000/mm³), relative microcytosis, high LDH, and slight elevations in the ESR and AST. Differential diagnoses included viral and mycobacterial infections, lymphoma, connective tissue disease, immunodeficiency, and protozoal infection. Whole body tomography showed multiple lymph nodes in the cervical region. A second stage Mantoux test, malarial smear, and an HIV test were unrevealing. Serologic immune markers only showed a past exposure to CMV. A BMA with flow cytometry showed a marginally hypocellular marrow without evidence for leukemia or lymphoproliferative disorder. The modal excisional biopsy showed effacement of its architecture with necrotic areas surrounded by reactive and foamy histiocytes consistent with histiocytic necrotizing lymphadenitis or Kikuchi Fujimoto disease. Immunohistochemical studies were confirmatory with positive immunostains for CD 3, 20, and 68. The patient was being managed supportively with antipyretics, fluids and analgesics prior to discharge.

Discussion: The exact cause for Kikuchi Fujimoto disease is unknown. It is thought to be an exuberant T cell response to multiple nonspecific stimuli. The course subsides from a few weeks to 6 months. There is recurrence in 3% of cases. On complication is progression to SLE. The typical presentation includes lymphadenopathy, fever, night sweats, weight loss, fatigue, chills and polyarthriti. The disease could be confused with tuberculosis, malaria, lymphoma and lupus. An excisional biopsy with immunohistochemical testing is the gold standard. The medical management is mainly supportive.

Low Testosterone Levels in Males Evaluated for Autoimmune Disease. A. Kimel and R. Lahita. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

Females predominate with autoimmune disease. Males who present with various autoimmune diseases like lupus, Sjogren syndrome and autoimmune muscle disease are often found to have low levels of androgens. Some of these males also have hyperprolactinemia. Patients with autoimmune disease and Klinefelter syndrome represent one group where levels of androgen are decreased. A total of 26 males were sampled from a large outpatient autoimmune disease practice. These males included 8 with SLE, 2 with RA, 7 with primary APLS, and 9 with other conditions. 42% of the males sampled were found to have hypoandrogenemia. Under no circumstances did the referring physician have any insight into the accompanying syndrome and none of the referring doctors noted gynecomastia or other feminizing physical signs. The average level of testosterone in the affected men was 135 ng/dL ± 5. The normal range of testosterone in the general population is 260–1,000 ng/dL. Only 4 men were found to have elevated levels of serum prolactin. The largest group of men with low levels of androgen was the men with the diagnosis of anti-phospholipid syndrome. The predominate class of autoantibody found in these men were the APLS antibodies. These data strongly suggest that low levels of androgen predispose men to autoimmune disease and are important to measure on initial presentation.

The Adherence to HAART in HIV (+) Pregnant Women: Retrospective Study in Hudson County. H. Park, O.Odeyemi, D. Kim, J. Shah, M. Leekala, A. Obiefuna, A. Tochuku, E. Scarinci, and A. Grigriou. Department of Medicine, Jersey City Medical Center, Jersey City, NJ.

Introduction: It is known that adherence to highly active antiretroviral treatment (HAART) in HIV (+) women is generally higher during pregnancy period than after delivery. However, there is not enough studies to support this and the causative factors for declining adherence were not well identified. This is a retrospective study for HIV (+) pregnant women in hudson county to identify the change of adherence to treatment during and after pregnancy and to identify the causative factors.

Methods: Among the HIV (+) pregnant women who are seen at the Family Health Center, the charts of 25 women who gave birth between

2002 and 2005 were analyzed retrospectively. The demographics, duration of disease, parity, mode of transmission, family structure, history of substance abuse, trend of CD4 and viral load, type of HAART regimen and adherence before, during and after pregnancy were analyzed.

Results: During the pregnancy 19 out of 25 (76%) showed good adherence. However, after delivery, only 12 (48%) were still maintaining good adherence. The good and poor adherence groups were compared. There were no significant differences in race, age, parity and previous history of substance abuse in the two groups. Those diagnosed with HIV during pregnancy were more adherent to treatment than those diagnosed before pregnancy. The number of active substance abusers and number of homeless were higher in the poor adherence group. The identifiable major causative factors in declining adherence included active drug use, lack of awareness of the consequence, denial, mental illness, poor family support structure and other co-morbidities.

Conclusion: This study showed that there is significant decline in adherence to HAART in HIV (+) pregnant women after delivery. The poor adherence group could be a high-risk group who could potentially spread HIV in the community. Special intervention should be implemented to improve the adherence especially after delivery.

Appropriateness of Digoxin Use in Elderly Patients. H. Chughtai¹, C. Buzuski², N. Reyes² and M. Reiser¹, Departments of ¹Medicine and ²Nursing, Jersey City Medical Center, Jersey City, NJ.

Introduction: Previous studies have shown that digoxin may be overprescribed for elderly patients. We chose to study the appropriateness of digoxin use in elderly patients in Hudson County.

Methods: Cross-sectional study with patient survey and data analysis using descriptive statistics (frequencies). This preliminary data is based on 7 patients with a mean age of 81.7 years.

Results: 49.5% patients were taking digoxin for more than 5 years. Only 28.6% of the patients knew why they were on digoxin. 85.7% of patients were not aware of complications/side effects of digoxin. Of all the patients, only 71.4% had symptomatic heart failure. 28.6% patients had an exercise tolerance of more than 5 blocks, 14.3% patients had an exercise tolerance of less than one block and 57.1% of patient had an exercise tolerance of less than one block. 57.1% of patients were found to be concomitant ACE inhibitors, 14.3% on diuretics while using of B-Blockers was 42.9% in patients on digoxin. Regular cardiac rhythm was found in 71.4% of patient while irregular cardiac rhythm was found in 28.6% of patients. New York Heart Association functional class: 82.6 (class 1); 14.3% (class 2), 42.9% (class 3), 14.3% (class 4). Only 14.3% of all patients complained about symptoms suggestive of digoxin toxicity.

Conclusion: Our initial data confirms that many patients are on treatment with digoxin without being on maximal treatment with other first line drugs (diuretics, ACE inhibitors, B-blockers) making them susceptible to toxic side effects of digoxin. We plan to confirm our preliminary findings using data from 20–30 patients and also include echocardiographic parameters to confirm if patient truly need digoxin or not.

Queens Hospital Center

A Case of Pulmonary Cavitory Nodules in a Patient with Rheumatoid Arthritis Treated with Tumor Necrosis Factor Alpha Inhibitors. Jagruti Patel, Karen Mrejen-Shakin, Adriana Abrudescu, Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

Introduction: Rheumatoid arthritis is characterized by inflammatory synovitis involving symmetrical peripheral joints. Although the course of this multisystem disease may vary many patients progress to polyarticular destruction of cartilage with bone erosions.

Macrophages and cytokines contribute to synovial inflammation and bone erosions. Drugs targeted at inhibiting the effects of the cytokine TNF-alpha have been developed: a soluble p-TNF-alpha receptor-IgG1 fusion protein, etanercept; and monoclonal IgG1 antibody against TNF-alpha, the chimeric infliximab; and the recombinant fully human adalimumab.

We report a case of a female with seropositive rheumatoid arthritis who developed pulmonary nodules when started on TNF-inhibitors.

Case Report: A 71-year-old female with a history of seropositive erosive rheumatoid arthritis (RA) who had failed various therapies, including methotrexate; was started on Etanercept 25 mg twice weekly in 2002. PPD and a chest radiograph were normal. The following month the patient improved, having less joint pain, morning stiffness, and requiring less than 5 mg/day of prednisone. Approximately 8 months later, while on etanercept, the patient's rheumatoid arthritis flared and the decision was made to

switch to adalimumab. The patient had improvement in the pain, stiffness and swelling of the hands, knees and ankle joints. After five months on adalimumab, the patient complained of cough, and fever. A chest radiograph revealed new cavitory pulmonary nodules. Repeat PPD was negative. CT scan of the chest showed diffuse thin walled cavitory nodules of different sizes. In November 2003, she had both a non-diagnostic fiberoptic bronchoscopy biopsy and CT-guided fine needle aspirate of the nodules. Cultures and acid-fast bacilli were negative. Adalimumab was discontinued and due to polyarticular pain, the patient was restarted on high dose steroids. At this point the patient had no pulmonary complaints and refused surgical biopsy of the nodules. Of note, since her rheumatoid factor, which was persistently positive prior to etanercept therapy, remained negative during both etanercept and adalimumab therapy, this excluded the possibility of rheumatoid nodules.

Repeat CT of the chest three months later showed that the nodules were getting smaller in size. In July 2004, because of relapsing polyarthrititis, the patient was rechallenged with etanercept. Although the patient had no pulmonary complaints, a follow up CT of the chest in October 2004 revealed changes in the pulmonary nodules. Etanercept was discontinued. On January 10, 2005 a video-assisted thoracoscopic wedge resection of the left upper lobe and the lingula showed benign cavitory and non-cavitory necrotic lesions with inflammation. Acid fast bacilli cultures were negative. Since broth culture grew staphylococcus aureus and tissue culture grew pseudomonas aeruginosa, workup for an infectious source was done. Transesophageal echo, blood cultures, and gallium scan were negative. Empiric antibiotics were started with no improvement in the nodules. Subsequently, the patient was treated with Prednisone, average daily dose between 10–20mg/day. Follow-up CT scan showed slight decrease in the size of the lung nodules.

Discussion: The cause of rheumatoid arthritis is unknown. Patients have hyperplastic synovial membranes, with increased vascularity and inflammatory cells, primarily CD4+T-cells. Anti-TNF-alpha drugs such as etanercept, infliximab, and adalimumab have been developed. These drugs have rare, although significant, side effects: reactivation of mycobacterium tuberculosis complex disease, mycobacterium avium-intracellulare complex disease, and a non-specific lung injury characterized by non-caseating granulomas.

Since our case demonstrated a temporal cause-and-effect relationship between the development of the pulmonary cavitory nodules and the treatment with TNF-alpha inhibitor medications, we suggest that these biologic drugs may also induce an inflammatory nodular-cavitory lung reaction.

Chronic Unexplained Diarrhea with Macroscopically Normal or Non-specific Colonoscopy Results. What Next? Kanwardeep Arora¹, Narayan Agrawal¹, Fred Rosner² and Svetlana Grinblat² ¹Department of Medicine, Queens Hospital Center, Jamaica, NY, and ²Department of Pathology, Elmhurst Hospital Center, Mount Sinai School of Medicine, New York, NY.

Introduction: Chronic diarrhea and abdominal pain is a common problem in the elderly and occasionally is difficult to diagnose etiologically. We discuss a patient who presented with chronic watery diarrhea and crampy abdominal pain, whose initial work-up was negative. The patient's biopsy showed collagenous colitis (C/C) initially thought of and treated as *Clostridium difficile* colitis.

Case Report: An 82-year-old obese Hispanic woman with hypertension, atrial fibrillation, and seizure disorder presented with chief complaint of diarrhea for 2 weeks. The patient was recently discharged from another hospital where she was treated with IV antibiotics. Diarrhea started three days after discharge and was characterized by multiple watery bowel movements/day associated with intermittent abdominal pain. Medications included Dilantin, zocor, digoxin, moxifloxacin and coumadin. Physical examination was non-contributory. Routine laboratory tests were normal. CT of the abdomen was non-specific. The patient was with flagyl, ceftriaxone, loperamide and prevacid. Colonoscopy was non-specific. *C. difficile* assay was negative. The patient improved symptomatically and was discharged but was readmitted after 2 weeks with similar watery diarrhea for 5 days. Biopsy taken during the previous colonoscopy was positive for collagenous colitis (CC) patient was started on mesalamine and cholestyramine. Patient was started on and zocor and prevacid were stopped because of their possible association with C/C was concurrently treated for *C. difficile*. Diarrhea resolved and the patient was discharged only on mesalamine. Currently the patient is asymptomatic.

Discussion: Microscopic colitis (MC), comprising of CC and lymphocytic colitis (LC) are uncommon entities. Characterized by chronic, watery, secretory diarrhea with a normal or near normal gross appearance of the colon on colonoscopy. It occurs most-commonly in the sixth decade of life. The rate of 9–10 % in different studies in patients with chronic watery diarrhea indicates the necessity to consider the diagnosis of MC in older individuals with diarrhea and normal colonoscopy. Biopsy is diag-

nostic, with CC the major microscopic characteristic is a thickened collagen layer 7–100 μm (normal: 1–7 μm) and with LC, an increase in the number of intraepithelial lymphocytes (IEL) often above 20 per 100 epithelial cells; (normal IEL: 3–5 per 100 epithelial cells). The pathogenesis of MC is unclear. Synchronous collagenous and pseudomembranous colitis have also been described, suggesting a possible etiologic role for *C. difficile*. MC has been linked to **simvastatin**, **lansoprazole**, NSAIDs, flutamide, ranitidine, gold salts and **ticlopidine**. The mechanism of the diarrhea is decreased absorption of sodium chloride accompanied by active chloride secretion.

Treatment is based mainly on anecdotal studies. Possible offending drugs should be stopped and the antidiarrheal of choice is loperamide. Various therapies that have been bismuth include budesonide, sulphasalazine, cholestyramine and bismuth. A trial of bismuth, sulphasalazine or cholestyramine usually should be attempted before treating the patient with steroid therapy.

Conclusion: Microscopic colitis should be considered in an elderly person with chronic persistent watery diarrhea with normal or near normal colonoscopy. Multiple biopsies should be routinely taken for histopathology in such cases including biopsies of the right side of the colon thus increasing the diagnostic yield. The possibility of medication-induced MC should always be considered and the possible offending drug should be stopped and the effects observed.

Effect of Albumin Polymorphism on Thyroid Hormones. Michael Aninyei, Vijayatha Gundarapu, David Reich, Paul Kim, Fred Rosner, and Issac Sachmechi. Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY

Introduction: Thyroid hormones (T3, T4/TH) circulate in the blood bound to carrier proteins: thyroxine-binding protein (TBG), transthyretin (TTR), prealbumin and human serum albumin (HSA).

While 99.97% of T4 is bound in the following distribution: TBG-75%, TTR-15%, only 10% is HSA bound with 0.03% existing as free T4 (FT4). T3, on the other hand is 99.7% bound, though less avidly, with 0.3% free.

Because free thyroid hormones exist in equilibrium with its carrier proteins, any factor that affects the quantity/ quality of the carrier, invariably affects the pharmacokinetics and pharmacodynamics of TH. This is best exemplified in familial dysalbuminemic hyperthyroxinemia (FDH), an autosomal-dominant disorder characterized by increased total T4 (TT4), elevated FT4, normal TSH and T3 level, as measured by one or two step immunoassay. Some rare cases of increased T3 have been described. We describe a case of a patient with FDH presenting with symptoms of hyperthyroidism.

Case Report: A 79-year-old Hispanic man with a history of hypertension, schizoaffective disorder, benign prostatic hypertrophy and chronic renal insufficiency was admitted for evaluation of wide complex tachycardia found on his outpatient 24 hr holter monitor done to evaluate his complaint of frequent palpitations.

The patient acknowledged that he had had palpitations for several years and that he is always nervous. He also stated that this "nervousness runs in the family." There was no associated weight loss, unusual hair loss or visual changes. He also denied any neck mass/goiter, diarrhea or abnormal skin rash/thickening but stated that his hand always "shakes." He denied any chest pain or shortness of breath, either at rest or with exertion. He also denied any orthopnea or paroxysmal nocturnal dyspnea but complained of chronic leg swelling with no recent change. Exercise tolerance remained very good and unchanged.

On admission, endocrinology consult was called for evaluation of persistently increased TT4 and FT4 levels. Vital signs were stable and physical examination revealed only a mildly anxious elderly man with coarse tremors of the hands on extension. The rest of the examination was unremarkable. Sonogram of the thyroid gland showed bilateral prominent lobes, left greater than right. Thyroid I-123 uptake scan was 19.4% (NL 15-40%). It also showed a mildly enlarged but non-palpable lower pole of the left thyroid lobe with homogenous activity throughout the gland. Thyroid function tests (TFTs) were done using routine automated direct one step/two-step immunoassays. These showed normal TSH levels of 1.22 and 0.78 (NL 0.34–5.6 mu/mL); T3 levels were normal at 98.4 and 125.3 ng/dL (NL 87–178). However, TT4 and FT4 levels were increased: FT4 levels were 2.25 and 2.34 ng/dL (NL 0.58–1.64), TT4 levels were 17.58 and 18.69 (NL 6.09–12.2). Free T3 by equilibrium dialysis was 402 ng/dL (normal 230–420) and alpha subunit for pituitary hormone was less than 0.3ng/mL (NL<1.0). Free T4 by equilibrium dialysis was normal-2.1 ng/dL (NL 0.8–2.7)

Cardiac work up including echocardiogram, cardiac enzymes, stress test and telemetry monitoring was unremarkable. He was treated with a beta-blocker and discharged after being assured that his thyroid condition was benign.

Discussion: The above case report and thyroid function tests results fit the classic description of FDH, an autosomal-dominant disorder characterized by increased TT4, increased FT4 (as measured by one/two step immunoassay but normal by equilibrium dialysis), normal or rarely increased T3 and normal TSH. It is common among Caucasians, especially of Portuguese and Hispanic (Puerto Rican) descent with a reported incidence of about 1.8%. It was first described independently by henneman et al and Lee et al in 1979, and it wasn't until 1994 that Petersen and Sunthornthevarakul, independently of each other, identified the precise genetic defect.

The central problem is the presence in the serum of a naturally occurring mutated albumin. This missense mutation in the HSA gene results in the replacement of the codon 218, which is normally arginine, with histidine following a guanosine→adenosine transition in codon 218 in one of the two alleles. The effect of this mutation is an albumin with 10–15-fold greater affinity for T4 and a 5 fold greater affinity for T3.

Other mutations involving the same codon 218 and codon 66 have been described. Important in the differential diagnosis is a TSHoma—a rare condition characterized by increased or normal serum TSH and elevated thyroid hormone levels with a high alpha subunit. The patient is usually thyrotoxic and MRI usually shows a pituitary tumor/hyperplasia. Thyroid hormone resistance syndrome is another important differential, characterized clinically by goiter and elevated/normal serum levels of TSH and elevated TH. It is rare and inherited in an autosomal-dominant fashion. The primary defect in the majority of the cases is one or more mutations in the TH receptor beta.

Conclusion: Familial dysalbuminemic hyperthyroxinemia is usually benign and does not usually require treatment unless there is a concurrent different thyroid dysfunction. Because of the paucity of knowledge of this condition, particularly among non-endocrinologists, there is a tendency for inappropriate treatment including RAI, medications and thyroid surgery. Hence, the need for extensive education on this condition. **NL=normal level.

Empiric Management of Acute Dilated Cardiomyopathy Two Years in Retrospect. Keside Amaechi, Subrahmanya Siripurapu, Rakhil Rubinova, and Sharad Jaitly. Department of Medicine, Queens Hospital Center, Mount Sinai School of Medicine, Jamaica, NY.

Introduction: Dilated cardiomyopathy refers to disease of the myocardium with associated chamber dilatation and cardiac dysfunction. It may be sequel to a variety of insults to the heart or it may be idiopathic. Irrespective of etiology, the acute management of dilated cardiomyopathy is strictly clinically based.

We report a case of acute dilated cardiomyopathy, pericarditis and myocarditis in an 18-year-old male, which was successfully managed using only empiric therapy and still found to be clinically stable two years later.

Case Report: The patient is an 18-year-old black male Rugby player from England who presented at the emergency department with complaints of chest pain, palpitations and dyspnea. He denied fever, but had a "flu" infection about 4 months previously which resolved spontaneously. He had no coronary artery disease risk factors. He had a normal lung exam, 1st and 2nd heart sounds, but with added rub. Electrocardiogram showed widespread ST segment elevation, and troponin I was elevated. He was admitted to the coronary care unit for acute pericarditis. Echocardiogram showed ejection fraction of 25%, global hypokinesis, 4 chamber dilatation and in-chamber spontaneous echo contrast. Concomitant myocarditis was immediately suggested and patient was started on empiric treatment consisting of initial heparin, warfarin (with target INR 2.0), beta blockers, aspirin, angiotensin converting-enzyme inhibitors (ACEI) and digitalis, while subsequent echocardiograms and troponin I levels began to show improvement. Antibodies to mycoplasma, cytomegalovirus, coxsackie and echo viruses were negative as was the anti-nuclear antibody testing. A left heart angiogram and endomyocardial biopsy confirmed myocarditis, showing myocardial inflammatory cells with cellular necrosis on microscopy; and normal coronaries. Ten days later, his ejection fraction rose from 25–50% and he was discharged on low-dose ACEI and warfarin.

Discussion: The prevalence of dilated cardiomyopathy is estimated to be 36 / 100,000, and 80% are usually classified as idiopathic. At least 20% of patients have familial forms of the disease with mutations in genes encoding cytoskeletal or nuclear membrane proteins. This disease is genetically heterogenous in transmission and there is no evidence for routine formal testing. Most patients pursue an inexorably downhill course, and will die of heart failure or arrhythmia within 3 years of diagnosis. Spontaneous improvement occurs only with 25% of patients. Antiarrhythmics are best avoided because of their proarrhythmic potential, instead consider insertion of cardioverter-defibrillator in patients with symptomatic ventricular arrhythmias. Endomyocardial biopsy is usually not necessary, but it is

helpful in the recognition of secondary cardiomyopathies such as amyloidosis. In patients with advanced disease that are refractory to medical therapy, cardiac transplantation should be considered. Timely assessment and symptom-directed inpatient therapy is critical in improving outcome and mortality.

Conclusion: Dilated cardiomyopathy is the cause of approximately 25% of all causes of congestive heart failures and the primary indication for cardiac transplantation in the US. Retrospective studies over the past 20 years by Matsumura et al have shown a trend towards decreasing mortality with the increasing use of angiotensin-converting enzyme inhibitors, beta blockers, and the avoidance of antiarrhythmics. However, the value of simple supportive, and empiric therapy at the time of initial diagnosis is emphasized and could be the most important single factor in early stabilization of what is still largely an unknown disease.

Fibrillary Glomerulonephritis. Garima Gupta, Fred Rosner, and Stafford John. Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Introduction: Fibrillary glomerulonephritis (FGN) is a rarely diagnosed ultrastructural, immune-mediated entity characterized by infiltration of mesangium and glomerular basement membrane by fibrillary deposits that are negative on congo-red and thioflavin-T staining but are reactive for polyclonal IgG and C3.

Case Report: A 22-year-old woman was admitted to our hospital for progressively increasing leg swelling. Her physical examination showed uncontrolled hypertension and bilateral lower extremity pitting edema. Her laboratory values included: Blood urea of 5 mg/dL, serum creatinine of 0.6 mg/dL, total cholesterol of 448 mg/dL and LDL of 342 mg/dL, albumin 1.5 g/dL. Urinalysis revealed proteinuria of >300 mg/dL, with microscopic hematuria. At this time, work up for glomerulonephritis was started, 24-hour urinary protein excretion was 3.8 gms. Tests for autoimmune antibodies, which included anti double-stranded DNA antibody titer, anti-nuclear antibody titer, anti sm-RNP, anti -Sm antibody, anti-Ro, anti-La antibody were all negative. Laboratory workup failed to show a paraproteinemia, cryoglobulinemia or acute or chronic infection with hepatitis B and C. Renal ultrasound showed increased pararenal echogenicity of both kidneys with thickening of the cortex.

A renal biopsy was performed to evaluate the cause of the very significant proteinuria. Light microscopic examination showed diffuse increase in the mesangial matrix and hyaline material, which was periodic acid-schiff (PAS) positive and negative for thioflavin-T and congo-red stains. Only a rare lobule had a mild increase in mesangial cellularity. Many tubular loops showed membranous-like changes and extensive spicules and double contouring on the epithelial side. The renal tubules had a high profusion of hyaline droplets in the proximal tubular segments. The renal arteries and arterioles did not show any significant changes. Electron microscopy of the glomeruli revealed numerous non-branching fibrils measuring 21 nm in cross section located in the mesangium and many capillary walls. Some areas of glomeruli basement membrane were unremarkable while most contained numerous broad areas of fibrils that separated the podocyte from glomerular basement membrane. There was extensive effacement of the podocyte foot processes. Above-mentioned PAS positive and Congo-red and thioflavin-T stain negative amyloid-like deposition in mesangium under light microscopy which showed were non-branching fibrils of 21 nm in cross sections are collectively diagnostic of fibrillary glomerulonephritis.

Patient was treated with simvastatin for hyperlipidemia. The patient continues to have proteinuria with the 24 hr protein excretion increasing to 5.1 gm with stable blood urea and creatinine.

Discussion: FGN is an idiopathic glomerular disease characterized by randomly arranged congo-red negative fibrils of 16–24 nm in diameter. FGN needs to be differentiated from a related entity called Immunotactoid glomerulopathy (ITG) with larger microtubular deposits, usually > 30 nm in diameter arranged in a mostly tactoid manner. This is important because FGN is associated with a low incidence of systemic diseases whereas ITG has been linked to a high incidence of lymphoproliferative diseases and monoclonal gammopathy. The incidence of FGN is less than 1% in a renal biopsy series. The clinical course of FGN in previously-reported cases has varied from almost asymptomatic disease to fulminant renal failure. Symptomatic patients can present with proteinuria, hematuria, hypertension and renal insufficiency that progress over months to years. This disease entity does not respond well to corticosteroids or cytotoxic drugs and end stage renal disease develops within 2–4 years in about half the patients. Fibril deposition recurs in more than 50% of allografts but with benign course. Further studies of glomerular fibrillogenesis are needed to develop more effective treatments for this condition.

The Effect of Folic Acid on Thyroid Hormone Replacement. Asad Chaudhary, Afshin Tavakoly, Fred Rosner, and Isaac Sachemchi. Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Introduction: Folate is considered one of the nutrients that is essential for many biochemical reactions within the human body. Folate and its role in erythropoiesis have been emphasized. Likewise, folate deficiency and its after-effects have been, clearly associated with homocysteins loads. However, folate and its effect on preexisting hypothyroidism have not been discussed in the medical literature.

The patient under discussion is a 36-year-old Guyanese woman who was diagnosed with Hashimoto's thyroiditis and polycystic ovarian syndrome with positive anti-thyroid peroxidase antibody at the age of 27 years. She had been followed in the Endocrine Clinic since then. Her baseline health status was unremarkable, as she was an otherwise healthy middle age woman, with a height of 5'2", weight of 125 lbs with body mass index of 22, vital signs have always been within the normal range, BP= 110/125/6075 mmHg, PR=6878 bpm, serum TSH=1.732.28 mIU/mL in 2005.

Her outpatient medications included levothyroxine 100 mcg /day which was increased to 125 mcg/day for six days in a week, since a seven day regimen would cause palpitations. No EKG record of paroxysmal or consistent atrial tachycardia or atrial fibrillation was reported.

In May 2005, her TSH was found to be 1.76, which had trended down to this level with months of treatment with levothyroxine. Other laboratory findings were unremarkable. Since she decided to conceive a child, she was advised to take prenatal vitamins and folate and was discharged from the clinic with no further changes in her medications. On her subsequent visit, she was complaining of tiredness, muscle pain, cramps, slight weight gain. Physical examination showed only slow relaxation of deep tendon reflexes, which were otherwise symmetrical. However, her TSH level increased had from 1.76 to 11.76 mIU/mL. The patient said she was compliant with folate and prenatal vitamin pills and especially took her levothyroxine as prescribed. No reasonable explanation was apparent. However, folate was removed from her regimen other medications were continued as they were. On the next visit, the TSH decreased from 11.76 to 3.00 mIU/mL, symptomatically the patient felt better and physical examination was unremarkable.

Discussion: Concomitant administration of folic acid to a patient who was receiving levothyroxine for the treatment of hypothyroidism, with euthyroid status evidenced by normal TSH and FT4, resulted in deterioration of the thyroid status, symptomatically as well as by marked increase in TSH. This may be an incidental finding, yet a significant one. The mechanism may be multi factorial, either decreased absorption of levothyroxine from the gastrointestinal tract with concomitant administration of folic acid, or an increase in the clearance of levothyroxine. The answer is unknown. Prospective studies examining this issue are recommended.

Impact of the Diabetes Center Team on Metabolic Parameters of Newly Referred Patients. David Reich, Sumera Ahmed, Michael Aninyei, Paul Kim, Sangita Parab, Manjulatha Nukala, Giti Mansouri, Hildegarde Payne, Betti Meenattoor, Clarita Avaricio, Aliyamma Samuel, Fred Rosner, and Issac Sachemchi. Division of Endocrinology, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Background: Most studies have shown that the majority of diabetic patients do not achieve American Diabetes Association (ADA) guidelines for clinical care. Studies have also shown that improvement in glycemic, blood pressure, and lipid control can have a favorable outcome in terms of reduction of microvascular and macrovascular complications.

Queens Hospital Center (QHC), a municipal hospital in the City of New York, serves patients from varied ethnic groups that suffer a disproportionately high prevalence of diabetes and its complications. Many of the patients are uninsured, meaning they have to purchase diabetes-testing supplies out of pocket. Furthermore, many of the patients have low health literacy. These are all factors that can impede successful management of the diabetic patient.

Aims: To assess changes in metabolic parameters of newly referred diabetic patients not at ADA recommended care on one or more metabolic targets, after referral to the QHC Diabetes Center of Excellence.

Methods: This is a retrospective cohort study employing electronic medical record review of 425 newly referred diabetic patients to the QHC Diabetes Center from January 2004 to August 2005. These patients, upon initial visit to the diabetes center, were not at the ADA recommended level on at least one of the following ADA clinical guidelines: A1c, systolic blood pressure (SBP), diastolic blood pressure (DBP), serum triglyceride (TG) level, serum LDL cholesterol level or absence of nephropathy screening within the year preceding initial visit.

These patients were followed for a minimum of 3 months and a maximum of 1 year in the Diabetes Center. The mean changes in the

above-mentioned ADA metabolic parameters were calculated if the initial parameter failed to meet ADA recommended goals.

Statistical calculations, including paired t-tests to determine the p-value, were performed using the SAS software program.

Results: Of the 425 patients referred to the Diabetes Center, 374 (88%) had an A1c \geq 7% on initial presentation. Of these patients, the mean change in A1c was a reduction by 2.0% ($P < 0.0001$). For patients that had an initial A1c \geq 9%, the mean change in A1c was a reduction by 2.8% ($P < 0.001$). Of the 425 patients referred to the Diabetes Center, 246 (58%) had an initial LDL cholesterol level \geq 100 mg/dL. Of these patients, the mean change in LDL was a reduction by 40 mg/dL ($P < 0.0001$). Of these 246 patients, 116 had an initial LDL \geq 130 mg/dL, and the mean LDL decreased by 55 mg/dl in these patients ($P < 0.0001$). Of the initial 425 patients, 149 (35%) had an initial TG level \geq 150 mg/dL. The mean change in these patients was a decrease in serum TG level of 105 mg/dL ($P < 0.0001$). Of the initial 425 patients, 263 (62%) were not at the recommended goal systolic blood pressure (they had SBP \geq 130 mmHg), and the mean change in systolic blood pressure of these patients after referral to the Diabetes Center was a decrease of 18 mmHg ($P < 0.0001$). Of the initial 425 patients, 153 (36%) were not at the recommended goal for diastolic blood pressure (they had DBP \geq 80 mmHg), and the mean change in diastolic blood pressure of these patients was a decrease of 11 mmHg ($P < 0.0001$). Of the 425 initial patients, data on baseline urine microalbumin testing was obtained on 392 and 263 (67%) had a urine microalbumin screen within 1 year prior to referral to the Diabetes Center. Of the 33% that did not have screening for microalbumin on presentation to the Diabetes Center, 107 (82%) had a urine microalbumin screen done when they were referred to the Diabetes Center.

Discussion: Diabetic patients had statistically significant beneficial changes on many metabolic parameters after referral to the QHC Diabetes Center. Although many of the patients were probably still not at the actual ADA recommended goal for some, or, in some cases, all of these parameters, the changes seen would be expected to have a favorable long-term impact on diabetes-related complications. For example, a reduction in A1c of only 1% would be expected to reduce microvascular complications by at least 25% and macrovascular complications by about 15%. A reduction in LDL cholesterol of 30% would be expected to reduce macrovascular endpoints by at least 25%, and a 10 mmHg reduction in systolic blood pressure would reduce microvascular and macrovascular complications and the risk of death by 35%.

Conclusion: Diabetic patients referred to the Diabetes Center of Excellence had significant improvement of their metabolic parameters. The success of the findings of this study is the product of a team approach, involving physicians as well as diabetes educators and dietitians. Barriers that may prevent more diabetic patients from achieving favorable changes in metabolic parameters should be identified and addressed.

A Medical Dilemma: Intracerebral Hemorrhage in a Patient with Lupus Exacerbation. Can Herpes Simplex Virus Be a Cause of Intracerebral Bleeding? Asad J. Chaudhary, Garima Gupta, Fred Rosner, and Adriana Abrudescu. Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Introduction: In this era of better understanding, more treatment options and higher diagnostic modalities, sometimes diseases are not that simple.

Case Report: A 19-year-old man with no significant past medical history presented with progressively increasing swelling of all 4 extremities for 3–4 days and sharp chest pain, which was severe, non-radiating but increased with deep inspiration. Physical examination was significant for a blood pressure (BP) of 160/100 mm/Hg, pulsatile precordium, and painful movement of small joints of both hands. Initial laboratory tests showed proteinuria and anemia with a hemoglobin of 7.3 mg/dL. Erythrocyte sedimentation rate was increased to 145, rheumatoid factor was 87. Immunofluorescence assay for anti double stranded DNA antibody titer was elevated at 1: 160. Antinuclear antibody (ANA) titer was also elevated at the level of 1:2560 with a speckled pattern. Serum Complement 3 and Complement 4 were decreased to levels of 43 and less than 10, respectively. Considering the results of these tests, a diagnosis of systemic lupus erythematosus (SLE) was made. The patient was treated with antihypertensive therapy and 1000 mg of solu-medrol daily for 3 days. Renal biopsy was planned to assess the proteinuria. On the day of renal biopsy, the patient signed out against medical advice (AMA). One day later the patient presented with dizziness and headache and was found out to have a BP of 160/100 mm/Hg. He was not taking his antihypertensive medications. His blood pressure was brought under control with medications overnight but he again signed out AMA the very next day. One day later he again presented with "the worst headache of my life" and fever with right sided upper lip blister. His BP at that time ranged between 140–160/90. 100 mmHg, he had no neurological deficits but mild neck rigidity. CT scan of

the head showed right temporal hemorrhage with surrounding vasogenic edema. Dexamethasone (6mg IV q6hours) was given after an initial bolus for cerebral edema. Serum for anti HSV1 and 2 antibodies were positive for IgG against HSV type 1 (HSV1). Acyclovir was given empirically. Lumber puncture (LP) was discussed as an option to reach a definite diagnosis but was postponed due to cerebral edema. EEG was normal and MRI failed to show any mass lesion in the brain or any evidence of vasculitides, treatment with intravenous Acyclovir was given. Lumber puncture was done after repeat CT showed a decrease in the cerebral edema. The cerebro-spinal fluid was positive for antiHSV1 IgG and HSV by PCR was undetected. Acyclovir was continued for a total of 10 days as well as oral prednisone 60 mg daily.

Discussion: Systemic lupus erythematosus is a chronic, occasionally life-threatening, multi-system disorder. Herpes simplex virus type 1 causes fulminant necrotizing meningo-encephalitis distinguished from other encephalitides by its focal and often hemorrhagic nature. Specific anti viral therapy with acyclovir can significantly improve the prognosis.

Summary and Conclusion: Our patient is a young male who presented with active multisystem SLE and while receiving high-dose maintenance corticosteroid therapy developed right temporal brain hemorrhage which may have been due to herpes simplex infection. Despite the inconclusive herpes simplex laboratory investigations, the decision to treat herpes simplex infection was made and resulted in a significant clinical improvement. Our patient walked out of the hospital on his own feet and with a smile on his face.

Marijuana Abuse a Nexus between Spontaneous Pneumomediastinum and a Sleeping Beauty. Michael Aninyei, Praveen Ponnammreddy, Habibur Rahman, Ricardo A. López. Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Introduction: The association between pneumothorax, pneumomediastinum, subcutaneous emphysema and drug abuse is well described in the literature. Various mechanisms including Muller's maneuver and Valsalva maneuver during drug abuse have associated. We report the delayed onset of pneumomediastinum and subcutaneous emphysema after marijuana use in a sleeping 20-year-old male.

Case Report: JL presented to the Emergency Department with sudden onset of chest pain, tightness and shortness of breath that awoke him from sleep one hour prior to presentation. He also complained of worsening chest tightness with deep breathing and cough that was productive of yellow sputum but no fever or chills. He had similar episodes as a child that resolved spontaneously. He smoked marijuana about two hours prior to developing the symptoms, during which he had inhaled deeply against a "closed throat."

On examination he was anxious, tachycardic and tachypneic. Pulse oximetry was 92% on room air. There was no tracheal deviation but there was mild intercostal recession. Auscultation revealed diminished bilateral breath sounds with diffuse rhonchi and wheezing. Subcutaneous crepitus was present in the suprasternal notch, neck and upper chest. The rest of the exam was unremarkable.

CXR and CT chest revealed diffuse pneumomediastinum with subcutaneous emphysema. The patient was admitted to ICU and treated with supplemental oxygen and bronchodilators. Daily CXR's revealed progressive improvement and he was discharged with appointments for outpatient follow-up.

Discussion: Pneumomediastinum is classified as primary spontaneous (non-traumatic) and secondary (traumatic). The non-traumatic type is very common in young adults. It occurs in any condition that creates a gradient between intra-alveolar and surrounding interstitial pressure with resultant alveolar rupture. Two mechanisms include: over inflation and increased alveolar pressure, which commonly occurs in expiratory airflow obstruction and glottic closure as in intentional Valsalva maneuvers (e.g., inhalational drug abuse), asthma, prolonged violent coughing, parturition, etc.

Alveolar rupture resulting from a sudden reduction in interstitial pressure caused by extreme inspiratory effort and reduction atmospheric pressure as in rapid mountain climbing, sudden return to surface from diving or air travel.

Secondary traumatic pneumomediastinum is often associated with prior trauma with perforations of the air and or food passages. Examples include intubation, endoscopy, esophageal rupture, etc.

Alveolar rupture leads to interstitial emphysema where fine air bubbles track along the bronchovascular bundle, coalescing into larger air collections in the mediastinum that can spread along the fascial planes causing pneumomediastinum, pneumothorax, subcutaneous emphysema, pneumoretroperitonium and even pneumoperitonium.

Clinical manifestations include chest pain, cough, dyspnea, mediastinal crunch and subcutaneous crepitus. CXR usually shows lucency surrounding the heart mediastinum and bronchovascular bundles.

The majority of simple non-traumatic pneumomediastinum resolves spontaneously; however in some cases pleural and/or mediastinal decom-

pression may be required. Secondary traumatic cases are treated as necessitated by etiology.

Conclusion: The link between marijuana and PPM appears to be the Valsalva maneuver commonly employed during its use. Unexplained PPM should prompt a search for inhalational drug abuse. Symptoms may be delayed by hours as seen in our patient.

Massive Embolic Stroke following ERCP in a Patient with Atrial Fibrillation. Kalavagunta Satish, Nimesh Shah, and Farshid Radparvar. Department of Medicine, Mount Sinai Service at Queens Hospital Center, Jamaica, NY.

Introduction: Acute ischemic stroke is a well-known complication of atrial fibrillation (AF). Acute massive embolic stroke leading to brain herniation as a consequence of paroxysmal AF has rarely been reported.

Case Report: An 80-year-old woman was admitted to the surgical service with a complaint of abdominal pain suggestive of acute pancreatitis. Further work up comprising CBC, amylase level and abdominal ultrasound established a diagnosis of gall stone pancreatitis. An ERCP was recommended for which she underwent a cardiac evaluation for procedural clearance. EKG, echocardiogram and stress test were performed which revealed that she had paroxysmal atrial fibrillation. Patient developed a focal neurological deficit after ERCP. CT scan revealed a massive CVA involving the right side of the brain eventually leading to subfalxian herniation and death.

Discussion: In our patient the etiology of the stroke was thought to be of cardioembolic origin. One of the determinants of this outcome in atrial fibrillation is its duration. Several clinical trials have shown a reduction in the risk of stroke upon anticoagulation in paroxysmal AF. There has been no study comparing the severity of the neurological insults between the various types of AF.

Conclusion: We present a case of a massive CVA in a patient with paroxysmal atrial fibrillation. Our suggestion is that, irrespective of the duration of the paroxysms of AF an aggressive peri-procedural anticoagulant approach has the best outcome.

Polymyositis as Initial Presentation of Breast Cancer in a Patient with Primary Sjögren's Disease. Michael Aninyei, Ebima Okundaye, Fred Rosner, and Adriana Abrudescu. Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

Introduction: Polymyositis (PM) is an inflammatory myopathy associated with an increased incidence of cancer, though to a lesser degree than dermatomyositis. This increased incidence is further heightened by the presence of an additional connective tissue disease. We report a case of breast cancer presenting initially with polymyositis in a woman with Sjögren's disease.

Case Report: A 55-year-old woman with a history of primary Sjögren's disease, hypertension, diabetes mellitus, and a family history of a sister with breast cancer presented for a routine follow up in our rheumatology clinic, complaining of progressive proximal muscle weakness and pain of two months duration that was associated with frequent falls. She also complained of dry mouth, difficulty swallowing food and required "lots of water to push it down." There was no history of fever, odynophagia, cough or rash. There was no joint pain or swelling, no night sweats but the patient had defined weight loss.

Physical examination revealed decreased power/motor strength in both proximal lower extremities. She had a dry oral mucosa. There were no skin rashes and no joint inflammations. Reflexes, sensation, cerebellar functions were normal as were the cardiac, chest, breast and abdominal examinations.

Laboratory results showed elevated levels of creatine kinase-846 and aldolase-20. Serum anti nuclear antibody (ANA) was strongly positive as were the Ro and La antibodies, rheumatoid factor 152 and C reactive protein-10 were increased. Anti-Jo 1 antibodies were negative. Serum thyroid stimulating hormone (TSH), electrolytes and magnesium levels were also normal.

Chest roentgenogram and esophagram were normal. Non-contrast CT scan of the head, chest, abdomen and pelvis revealed pretracheal, precardiac and multiple enlarged bilateral axillary lymph nodes. Mammogram showed a new 1 cm ill-defined nodular density and a cluster of micro-calcifications in the inner lower quadrant of the right breast that later proved to be low grade ductal infiltrating carcinoma on biopsy with negative sentinel node sampling.

Quadriceps muscle biopsy showed increased fiber size variation with focally increased endomyosial fibrous connective tissue and lymphoplasmacytic infiltrate. It also revealed numerous strongly esterase-positive inflam-

matory cells in the endomyosial connective tissue. There was an abundance of T-cell and histiocytes but no B cells. The patient responded to treatment with steroids with resolution of her active polymyositis. She also underwent a right mastectomy and is currently receiving hormonal therapy.

Discussion: The temporal relationship between myositis and malignancy is well known. However, the etiology of this relationship is still mainly hypothetical. Compared to the general population, the incidence of cancer among patients with dermatomyositis (DM) and polymyositis (PM) was 15% and 9% respectively, in a Swedish study. This incidence was much higher-27% in patients with myositis and an additional connective tissue disease, as reported in a recent Australian study but still lower than that of DM-42%. Our patient belongs to this category in that she already had Sjögren's disease. Our case also remains a rarity among the published literature. The malignancy can occur prior to, at or after the onset of myositis, though the peak incidence is within 2 years prior to or after onset of myositis. Commonly associated malignancies include ovarian, bladder, gastrointestinal, cervical, pancreatic, non-Hodgkin lymphoma and nasopharyngeal cancers. Mammogram and pelvic exam should be performed in female patients with PM.

Conclusion: We present a patient with PM. Knowledge of the association of PM with cancer prompted an active search for malignancy that revealed the presence of breast cancer which was appropriately treated.

There is a need to actively search for malignancy in patients with PM or DM. This is the proper standard of care according to the American College of Rheumatology. The use of only routine screening tests may be inadequate to find the cancer.

Recurrent Chest Pain in a Young Woman. Diana Arévalo, Habibur Rahman, Ricardo López. Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Case Report: DC is a 33-year-old woman who presented with complaints of right-sided pleuritic chest pain and shortness of breath starting two days prior to her menses. She denied any other symptoms. Her medical history was significant for hemoptysis and a spontaneous right pneumothorax in her home country, Jamaica, W.I. in 2003 that subsequently was complicated by a hydropneumothorax. The pleural fluid was exudative and negative for infection and malignancy. She was treated initially with chest tube drainage but her lung failed to re-expand, and she developed a hemorrhagic hydropneumothorax prompting a fiber optic bronchoscopy and video assisted thoracoscopy. The bronchial tree was normal and washings were non-diagnostic. Thoracoscopy revealed hemorrhagic fluid and a collapsed right lung encased in a peel. Pleural biopsies revealed nonspecific inflammation. The right hemidiaphragm had fenestrations and hemorrhagic tissue over it, biopsies of which revealed endometrial glands and stroma. These findings were consistent with endometriosis. The patient's hospital course was complicated by an empyema, which was treated with antibiotics, decortication and pleurodesis. She was then started on Depo-Provera 150 mg via intramuscular injection monthly for six months. After six months of treatment, the patient developed a pulmonary embolus following a long car ride. She was treated with anticoagulant therapy for six months and the hormonal therapy was discontinued. The patient remained asymptomatic until presenting with her current presentation.

Her physical examination during her recent admission was significant for reduced breath sounds on the right with dullness to percussion. Her CBC revealed mild microcytic anemia and her serum chemistry was normal. A spiral CT was negative for emboli, but demonstrated a loculated right pneumothorax without air-fluid levels, ipsilateral mediastinal shift and a loculated pleural effusion consistent with a trapped lung. Lower extremity Doppler ultrasound did not identify any thrombus. The patient's symptoms resolved with analgesics. The patient was discharged home, with continued follow up in the Chest clinic. PFTs three months after discharge revealed an insignificant tendency toward restrictive changes with preserved gas exchange. The patient continues to have recurrent chest pain preceding her menstrual cycle that responds to analgesics.

Discussion: Thoracic endometriosis is a rare occurrence with 110 cases reported over 28 years. Of these, the most common presentation was pneumothorax in 73%, followed by hemothorax in 14%, hemoptysis in 7%, and lung nodules in 6%. Chest pain is the most common symptom and is present in 90% followed by dyspnea in 33%. Histopathologic demonstration of thoracic endometrial tissue is not always necessary, diagnosis is usually clinical and therefore requires a high index of suspicion. Treatment is usually hormonal suppression of ovulation, if it is unsuccessful or if the patient cannot tolerate hormonal therapy then pleurodesis is usually successful. Despite therapy, most patients continue to experience catamenial chest pain as in our patient.

Conclusion: Thoracic endometriosis is a rare entity among women of childbearing age; its diagnosis requires a high index of suspicion. Recurrent chest pain is common despite appropriate therapy; physician

awareness of this fact will preclude unnecessary and potentially harmful diagnostic testing.

Refeeding Syndrome—Underdiagnosed and Undertreated. Chinar Mehta, Heather McKenzie, Valeriy M. Vilensky, and Ricardo A. López. Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Case Report: LE is a 68-year-old man who presented with recurrent falls, generalized weakness, and poor oral intake of 4–6 weeks duration. Recurrent falls he attributed to being weak; his knees gave up on attempts to ambulate. He had lost 60 lbs in the last 3 months. Past medical history includes depression and peripheral vascular disease. Physical examination revealed an emaciated elderly man. A 6 × 5 cm ulcerated, foul smelling skin lesion with surrounding erythema was noted on his left temple, later diagnosed as a sebaceous carcinoma. He had dry gangrene of the toes of his right foot and absent pedal pulses. WBC was 19K with 4% bandemia. Serum prealbumin was 1.2 mg/dL (normal = 16–30 mg/dL), albumin was 1.2 g/dL (normal = 3.5–5.2 g/dL), and remaining blood chemistries were unremarkable. CXR and head CT were unremarkable. An evaluation for metastatic spread of the skin cancer was negative.

Intravenous antibiotics were administered for cellulitis surrounding the skin lesion. Surgical consultants were called for possible tumor resection and foot amputation.

Dietary consult for malnutrition was obtained and a caloric count revealed that the patient was only consuming 50% of his goal calories, despite oral supplements and feeding assistance from the nursing staff. Enteral nutrition via nasogastric tube was initiated with a prescription containing 1,809 cal/day (34 cal/kg IBW), 109 g of protein (1.6 g/kg IBW), (28 NP cal/kg IBW) and 1,392 cc of total volume.

The next day patient was found to be in acute respiratory distress. Serum chemistries revealed hyponatremia, hypokalemia, hypomagnesemia, and hyperglycemia. CXR showed congestive changes. The patient was transferred to the MICU, where he was treated with antibiotics, an insulin infusion, electrolyte supplementation, and intravenous hydration. He clinically improved after the tube feeds were held and the electrolytes corrected, but later he developed progressive mental status changes requiring intubation for airway protection. He continued to deteriorate and expired after cardiopulmonary arrest.

Discussion: Refeeding syndrome (RFS) is a metabolic complication that occurs in patients who have undergone a period of starvation and are started on aggressive enteral or parenteral nutrition. RFS occurs in up to 0.8% of hospitalized patients and can be as high as 30–38% with TPN.

In RFS, the body shifts from protein and fat catabolism to carbohydrate metabolism. Glucose becomes the primary fuel source. This stimulates an increase in insulin production which leads to increased cellular uptake of glucose, phosphate, magnesium, and potassium leading to decreased serum concentration of these ions. These metabolic derangements can lead to cardiac, respiratory, and neuromuscular dysfunction, and even sudden death.

It is therefore recommended that the daily caloric intake in severely malnourished patients initially not exceed 15 cal/kg, with no more than 100 g of carbohydrates and 1.5 g/kg of protein. Electrolytes should be replaced liberally. Fluid intake should be limited to 800 cc/day plus maintenance for insensible losses. Caloric intake can then be gradually increased after the first week with a goal weight gain of 1.5 kg/wk or 0.25 kg/day.

Conclusion: RFS is an underdiagnosed and undertreated condition which can be potentially fatal if not recognized, when severely malnourished patients are fed aggressively. Joint efforts by medical, nursing, and dietary staff can prevent this fatal but preventable condition.

Retained Peritoneal Glossybiboma Mimicking Angina Pectoris. Ebima Okundaye, Micheal Aninyei, Julio Vaquerano, Leelavathi Kasturi, Fred Rosner, and Henry Safier Henry. Department of Medicine, Mount Sinai Services at Queens Hospital Center, NY.

Introduction: Intra-abdominal foreign bodies, following open surgical procedures have been reported on numerous occasions. One of the foreign bodies inadvertently left in open abdominal surgeries is the gauze sponge. The gauze sponge, a cotton derivative, serves primarily as a blood-mopping device in surgical procedures. Retained gauze sponge (glossybiboma) can cause symptoms related to its mechanical presence.

Case Report: We present a 56-year-old man, with a history of hypertension, non-compliant with his medications, and a history of cholecystectomy 10 years prior. He presented with exertional chest pain radiating to the left arm and epigastrium. The patient underwent a cardiac workup including serial EKGs, cardiac enzymes and stress test, which

showed normal myocardial perfusion. The patient was discharged but was readmitted with recurrent symptoms. An esophagogastroduodenoscopy was performed and *H. pylori* negative gastritis was found.

CT scan of the abdomen revealed a mass lesion on the lesser curvature of the stomach extending to the left lobe of the liver. A subsequent exploratory laparotomy showed an encapsulated fibrinous mass adjacent to the stomach, which was excised along with a portion of the adjacent gastric wall. Histology revealed a 10×5×4 cm gauze sponge with secondary granulomatous changes and evidence of focal and purulent material secondary to involvement of the gastric wall.

Discussion and Conclusion: Retained gauze sponge following surgery may produce a clinically symptomatic radiologically apparent mass lesion. This diagnosis should be considered in the differential diagnosis of chest pain radiating to the epigastrium in a patient with a history of abdominal surgery. To our knowledge, this is one of the few cases of a glossybiboma gauze sponge causing symptoms after a long period of clinical dormancy and is unique because of its presentation as substernal chest pain radiating to the left arm and epigastrium.

Streptococcus gordonii Septic Arthritis and Endocarditis in a Patient with Rheumatoid Arthritis Receiving Etanercept Therapy. Alexander Mbewe, Adriana Abrudescu, Seong K. Choi, Fred Rosner, and Lambert King. Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

Introduction: Septic arthritis is a medical emergency which, if not promptly treated can lead to significant morbidity and mortality. Prompt recognition and treatment are critical to ensure a good prognosis. Several risk factors predispose selected patients to septic arthritis such as age greater than 60 years, diabetes mellitus, a remote focus of infection, intravenous drug use, immunosuppression, presence of inflammatory arthritis, joint trauma and/or the presence of a prosthesis. We describe an elderly patient with long-standing rheumatoid arthritis (RA) who developed streptococcus septic arthritis and endocarditis while on treatment with etanercept for RA.

Case Report: A 61-year-old woman with a long standing history of seropositive RA presented with three days of increased pain and swelling of the left knee.

Medical history was significant for rheumatoid arthritis for the last 14 years, rheumatic heart disease, hypertension, prior cerebrovascular accident, asthma and seizure disorder. She had no history of recent dental work. She has been treated with etanercept and hydroxychloroquine for the past three years and her RA was in remission.

On physical examination, she was febrile at 101° degrees centigrade, had tachycardia of 109/min, with normal blood pressure. There was no evidence of dental caries. There were no skin rashes or skin infarcts. There was a grade 2/6 systolic murmur over the mitral area. There was no hepatosplenomegaly, and no lymphadenopathy. The left knee was swollen, warm, tender with a large synovial effusion and severe functional impairment. Initial laboratory findings: white blood cells 9,700 with 82% neutrophils, and erythrocyte sedimentation rate of 128 routine serum chemistries and liver function tests were normal as was the urine analysis. Approximately 100 mL of purulent fluid was aspirated from the left knee. The joint fluid had a white blood cell count of 127,000 (92% polys, 3% lymphocytes, 5% monocytes) glucose 20 mg/dL, and protein 3.7mg/dL.

Blood cultures and synovial culture results were positive for *Streptococcus gordonii* (the streptococcus viridans class), sensitive to vancomycin, ceftriaxone, erythromycin, clindamycin, and chloramphenicol.

Transesophageal echocardiography was done which revealed a thickened mitral valve with severe mitral regurgitation and a thin mobile vegetation measuring 1.2 cm in length, consistent with endocarditis.

The patient was treated with vancomycin serum levels were in the therapeutic range. The patient developed new onset expressive aphasia and right-sided hemiplegia. A repeat head CT showed a hemorrhagic stroke and mitral valve surgery was deferred due to the risks associated with anticoagulant therapy. The patient was transferred to a rehabilitation unit with antibiotics being continued for a total of three months.

Discussion: Etanercept is a competitive inhibitor of tumor necrosis factor (TNF) at the cell surface receptor and regulates the biologic activity of TNF. There is concern regarding the vulnerability to infection in patients treated with TNF inhibitors.

Streptococcus viridans is a heterogeneous group of streptococci which are normal flora found in the human nasopharynx and gastrointestinal tract and commonly found in dental caries and subacute bacterial endocarditis (SBE), especially in previously damaged valves such as in rheumatic heart disease. However, it is uncommon to find viridans streptococci in septic arthritis.

In our patient, it is likely that an already structurally compromised rheumatic mitral valve was the initial focus of infection, with seeding probably originating from the patient's oral flora. Subsequent systemic dissemination then led to left knee septic arthritis and cerebrovascular

embolic phenomena. However, the rapidity of systemic spread over a period of five days, despite adequate antibiotic therapy, may have been due to an immunocompromised state secondary to prior etanercept therapy. To our knowledge this is a unique case report of *S. gordonii* septic arthritis in a rheumatoid arthritis patient treated with etanercept.

Intestinal Pseudo-obstruction as the Initial Presentation of Systemic Lupus Erythematosus in a Male Patient. Jonathan Marquez, Fred Rosner, and Adriana Abrudescu. Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

Introduction: Systemic lupus erythematosus (SLE) is a disease with multi-system involvement which presents with a myriad of clinical manifestations, signs and symptoms. Although it is common for SLE to present with rash, ulcers, arthralgias, or systemic symptoms such as fever or fatigue. We present a rare case of intestinal pseudo-obstruction as an initial presentation of SLE.

Case Report: A 33-year-old African-American man with no significant past medical history presented with cramping left lower quadrant abdominal pain with anorexia, nausea and vomiting for two days. The patient had no melena, hematochezia, or hematemesis. There was no history of recent travel, no sick contacts, no recent intake of medications or new food items, and no history of surgery. The patient has a 5-pack-year smoking history, but denied illicit drug use or alcohol intake. On physical examination, the patient was ill-appearing, tachycardic and hypertensive but afebrile. He had no skin rashes, no oral ulcers, no palpable lymphadenopathy, and no joint swelling. His chest was clear, and his heart examination was normal. On abdominal exam, the patient had direct and rebound tenderness with guarding over the left lower quadrant, hypoactive bowel sounds. Rectal exam showed good sphincter tone, no tenderness, with guaiac-negative brown stool.

Pertinent laboratory tests including a complete blood count showed only mild thrombocytopenia. Routine serum chemistries were normal as were serum electrolyte levels and renal function, was liver function tests revealed mild elevations of AST and GGT and LDH, along with hypoalbuminemia of 1.9. Urinalysis showed protein of more than 300 mg/dL with occasional coarse granular casts. Serum amylase level was normal. Abdominal CT scan showed moderate ascites and small bowel loops with a thick and moderately distended appearance. The patient underwent exploratory laparotomy with the initial impression of acute abdomen / small bowel obstruction. During the procedure, a small proximal jejunal volvulus was identified and detorsion was performed.

Three days after the surgery, the patient developed fever, nausea, vomiting and increasing abdominal pain. Repeat abdominal CT scan demonstrated bilateral pleural effusions, moderate ascites, thickening of loops of small bowel, and a horseshoe kidney. Blood count revealed leukocytosis, anemia and worsening thrombocytopenia. The patient was also noted to have deterioration of renal function with BUN / creatinine increasing from 19/1.4 on admission to 75/4.7 with nephrotic-range proteinuria. Further work-up revealed positive serum anti-nuclear antibodies with a titer of 1:320 showing a homogenous pattern, decreased complement levels, positive anti-double stranded DNA antibodies, and positive anti-Smith antibodies. The diagnosis of SLE was made since the patient satisfied seven of the eleven American College of Rheumatology Revised Criteria for Classification of SLE. The patient was started on steroid therapy with dramatic clinical improvement along with resolution of anemia, thrombocytopenia and renal failure.

Discussion and Conclusion: Systemic lupus erythematosus is most prevalent in the 20–40 year age population with a female to male ratio of 9:1. Gastrointestinal complications of SLE include small and large intestinal vasculitis, and ischemic enteritis which may progress to bowel infarction, pancreatitis, inflammatory bowel disease, celiac disease and protein-losing enteropathy.

Intestinal pseudo-obstruction has been very rarely reported in association with systemic lupus erythematosus, and usually in patients with a long duration of the disease and multiple organ involvement. Our patient is unique because of SLE in a man and a two-day history of abdominal complaints and no other associated symptoms suggestive of SLE on initial presentation.

Tenofocir-Related Renal Fanconi Syndrome. Garima Gupta, Erfifida Restrepo, Fred Rosner and Stafford John. Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

Introduction: We report a case of rarely diagnosed Fanconi syndrome associated with tenofovir fumarate, a nucleotide reverse transcriptase inhibitor with anti-HIV therapeutic effect.

Case Report: A 53-year-old HIV-infected woman was referred to our immunology clinic for HIV treatment in January 2005. She had previously received one antiretroviral regimen and was on didanosine (250 mg QD), tenofovir (300 mg QD) and efavirenz (600 mg QHS) since February 2004. She was continued on this antiretroviral regimen. On this visit, she presented with complaints of weakness, fatigue, weight loss of about 20 lbs in the last 3 months and bony pain in both lower extremities. Physical examination showed a body weight of 123 lbs, Blood pressure of 127/78 mmHg with marked muscle atrophy. Her initial laboratory workup was significant for hypokalemia. Her presenting complaints were initially attributed to AIDS. On follow-up visits, she continued to have persistent weakness and fatigue. Further laboratory investigations revealed the following constellation of abnormalities: serum potassium 3.2 meq/L, serum bicarbonate 19 meq/L, serum phosphate 1.1 mg/dL, serum glucose 102mg/dL, serum calcium 8.4 mg/dL, urea 8 mg/dL, serum creatinine 0.9 mg/dL, serum lactic acid 2.4 meq/L. Urinalysis was significant for PH of 7.00, glycosuria (urine glucose level 250 mg/dL, proteinuria (dipstick 1+). Liver function tests showed the serum alkaline phosphate to be increased to 398U/L with a reduced serum albumin level of 3.4 gm/dL.

The presence of hypophosphoremia with mild hypocalcemia along with persistent bony pain in the lower extremities prompted further testing to rule out metabolic bone disease. Serum 25-hydroxy vitamin D level was reduced to 15 ng/mL, intact parathyroid hormone level was increased to 106 pg/mL. Bone densitometry was significant for osteoporosis.

Discussion: Considering this metabolic picture with a non-anion gap metabolic acidosis, normoglycemic glycosuria, proteinuria, hypophosphoremia and mild hypocalcemia, the diagnoses of Fanconi syndrome and vitamin D deficiency were made in March 2006. Antiretroviral treatment including Tenofovir was discontinued and the patient treated with vitamin D, bisphosphonates, potassium phosphate and calcium carbonate. Two weeks later, patient reported to have less in fatigue and weakness with improvement in her exercise tolerance. We anticipate that her electrolyte imbalance will improve with the above interventions.

Summary: This case demonstrates tenofovir-induced Fanconi syndrome with hypokalemia, normoglycemic glycosuria, proteinuria with non-anion gap proximal renal tubular metabolic acidosis.

The mechanism of proximal renal tubular dysfunction is secondary to cellular accumulation through increased entry from human organic anion transporters (hOAT) located on the basolateral side of the tubule and decreased efflux into the tubular lumen mediated by multidrug-resistance-protein (MRP-2). Protease inhibitors can also inhibit MRP-2 thereby decreasing efflux of tenofovir. Patients receiving combinations of tenofovir and protease inhibitors should be closely monitored for the development of proximal renal tubular toxicities.

Conclusion: Nephrotoxicity of tenofovir should not be underestimated. This fact becomes more important in view of AIDS patients, where serum creatinine may not increase but timely examination of serum electrolytes and urinalysis will guide the medical staff into making the correct diagnosis.

The Effect of Proton Pump Inhibitors on Serum TSH Levels in Euthyroid Patients on Levothyroxine. Issac Sachmechi, Michael Aninyei, David Reich, Garima Gupta, Francisca Wibowo, Natalia Yurkovetsky, Ebima Okundaye, Chinara Mehta, Jagdish Kandala, Fred Rosner, and Paul Kim. Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

Introduction: Several medications are known to affect the level of serum thyroid hormone in hypothyroid patients on levothyroxine (L-T4) replacement either by reducing gastrointestinal absorption of L-T4 or increasing its metabolic clearance. Proton pump inhibitors (PPIs) are commonly used; their effect on L-T4 absorption or metabolic clearance in humans is not known.

We have observed an apparent rise in thyroid stimulating hormone (TSH) levels in hypothyroid patients on L-T4 replacement who were later started on PPIs.

Objective: This study was designed to retrospectively examine the effect of PPIs on TSH values in hypothyroid patients with normal TSH levels on L-T4 replacement.

Methods: The data collection was done by retrospective electronic medical record review from the period of December 2002 to August 2005 on patients with hypothyroidism who were on at least 50 mcg daily L-T4 replacements at Queens Hospital Center.

The study group (n=40) patient data was collected by reviewing and randomly selecting euthyroid patients with history of hypothyroidism on stable L-T4 replacement for at least six months who were later started on a PPI. TSH levels were collected prior to and at least one month after the PPI was started.

The control group (n=71) patient data was collected by reviewing TSH levels among randomly selected euthyroid patients with history of hypothyroidism on stable L-T4 therapy and not on a PPI during the same period as the study group's data was being examined.

The statistical analysis was done by comparing the mean change in TSH level in each group using the paired test (SAS 6.2 Version).

Results: In the study group, the mean increase in TSH level, 1.3 mIU/mL \pm 0.63, was statistically significant ($p < 0.05$). In the control group, the mean change in TSH level, 0.007 mIU/mL \pm 0.06, was not statistically significant ($p = 0.95$).

Discussion: The results of the study showed that the use of PPIs in hypothyroid patients on L-T4 replacement significantly affect the level of serum TSH. In animal studies, PPIs were found to increase metabolic clearance of L-T4 by enhancing the activity of the enzyme, L-T4 glucuronyltransferase, that is responsible for glucuronidation of thyroxine. We assume this is the most likely mechanism also in humans, although suppression of gastric acid secretion by PPIs might affect the absorption of L-T4.

Conclusion: To our best knowledge, this is the first study in humans with hypothyroidism demonstrating the effect of PPIs on the metabolism of thyroid hormone. PPIs should be added to the list of medications affecting the level of thyroid hormone in hypothyroid patients treated with L-T4 replacement. Hypothyroid patients with normal TSH values on L-T4 replacement will need additional thyroid function testing following the treatment with PPIs and may need adjustment of L-T4 dose.

Unusual Onset of Acute Rheumatic Fever. Ebima Okundaye, Saurabh Chhabra, Elena Korniychuk, Jean-Louis Dupiton, Fred Rosner, and Adriana Abrudescu. Department of Medicine, Queens Hospital Center, Mount Sinai School of Medicine, Jamaica, NY.

Introduction: Acute rheumatic fever is an immunological sequel of streptococcal sore throat infection. It is a common pathology in children and young adults. It rarely occurs above middle age. There are rare reports of its occurrence in the elderly population. The symptoms usually arise within 1–4 weeks after the streptococcal sore throat infection.

Case Report: A 67-year-old woman presented with complaints of malaise, low-grade fever, migrating joint pains and rash of 3 weeks duration. The fever was low grade, not associated with chills, but no temperature was taken at home. The joint pains initially started on the right wrist but later migrated to the left wrist and both ankles. The pain was associated with swelling and warmth and rash over the joints. The patient had associated lethargy and weakness.

The patient gave a history of hypertension, hyperlipidemia and osteoporosis. She had a recent vacation in Mexico 4 months prior where she developed sore throat associated with diarrhea. Both were treated symptomatically and resolved after one week. No antibiotics were given. The patient lives with a daughter and grandchildren.

Physical examination showed an obese woman with marked conjunctival injection, grade -1 leg edema and tenderness in the left wrist and both ankles on movement. There was an erythematous skin rash on the involved joints that blanched on pressure application. Heart auscultation was significant for a grade -1 diastolic murmur over the mitral area.

The patient had an increased white blood cell count with marked neutrophilia. Liver function tests revealed markedly elevated enzymes; erythrocyte sedimentation rate and C-reactive protein were both elevated. Though beta streptococcal throat culture was negative, the serum streptozyme titer was 1:400, and an antistreptolysin -O (ASO) titer was 1:1097. Anti-nuclear antibodies and Rheumatoid factor were both negative. EKG was unremarkable and there was trace protein in the urine.

The patient was diagnosed and managed for acute rheumatic fever. Aspirin and benzathine penicillin stat dose were given two days after admission. Her symptoms improved, as did the physical findings. The patient was discharged on the fifth day after admission.

Discussion: Acute rheumatic fever is an antibody-mediated reaction to streptococcal infection; it is characterized by specific of symptoms and signs. The modified Jones criteria require any two of the major criteria of carditis, erythema marginatum, subcutaneous nodules, migratory polyarthritis and chorea; or one of the major criteria and two minor criteria such as elevated ESR, C-reactive protein, prolonged PR interval, arthralgia and fever, in addition to evidence of beta streptococcal infection. Our patient had the major criterion of migratory polyarthritis and two minor criteria of elevated ESR and fever, in addition to evidence of streptococcal

throat infection in that the serum streptozyme and ASO titers were increased.

Summary and Conclusion: The syndrome of acute rheumatic fever is common in children due to the high proliferation of antibodies in that population. The most important complication of streptococcal infection is rheumatic heart disease. Few case reports have described rheumatic fever in the adult population. Perhaps, due to the mature differentiation of the immunoglobulin lineage in this age population at the time of streptococcal sore throat infection. This diagnosis should be considered in patients with polyarthritis in the elderly age group. This case is unique not only in terms of the late age of occurrence but the prolonged latent period between the streptococcal infection and the onset of the immune-mediated acute rheumatic fever.

Use of Early Aggressive Therapy in the Management of Life-Threatening Microscopic Polyangiitis: A Successful Approach. Keside Amaechi, Karen Mrejen-Shakin, Robert Murithi, and Adriana Abrudescu. Department of Medicine, Queens Hospital Center, Mount Sinai School of Medicine, Jamaica, NY.

Diffuse alveolar hemorrhage is characterized by bilateral alveolar infiltrates on chest radiograph, iron deficiency anemia, and hemoptysis. Diagnosis is confirmed by fiberoptic bronchoscopy revealing increasing amounts of red blood cells and hemosiderin-laden macrophages. Antineutrophil cytoplasmic antibodies (ANCA) related small vessel vasculitis commonly present as a rapidly progressive glomerulonephritis and alveolar capillaritis. We report a case of a patient with perinuclear-ANCA positive microscopic polyangiitis who presented with life-threatening pulmonary and renal hemorrhage successfully managed by early treatment with pulse dose corticosteroids, plasmapheresis and cyclophosphamide.

Case Report: A 55-year-old male from Haiti with a past medical history of well-controlled diabetes and hypertension presented to the Emergency Department with complaints of urinary urgency and dry cough for about one week. Urinalysis showed microscopic hematuria and he was told to follow up with his doctor. One week later, he came to our Emergency Department complaining of dry cough with shortness of breath and "pink urine." Vitals were stable. Chest radiograph showed bilateral alveolar pulmonary infiltrates, and serum chemistry now revealed renal insufficiency, (BUN 58 mg/dL, creatinine 6.9 mg/dL). While in the Emergency Department he spiked to 101.° F. He now coughed up large amounts of bright red blood with large clots, and had gross hematuria. The patient became lethargic and hypoxic with a room air saturation of 68%. He was rapidly intubated and admitted to the intensive care unit. Repeat chest radiograph showed significant progression of alveolar infiltrates. On 100% oxygen and low tidal volumes the arterial blood gas was 7.38/40/81. Due to the life threatening hypoxia, broad-spectrum antibiotics, pulse dose intravenous corticosteroids, plasma exchange transfusion, and cyclophosphamide were started within 24 hours. Bronchoscopy confirmed diffuse alveolar hemorrhage. Serum ANA and anti-glomerular basement antibody were negative. P-ANCA (antimyeloperoxidase) was positive (100 U/mL). Kidney biopsy revealed crescentic glomerulonephritis with pauci-immune deposits on electron microscopy, confirming the diagnosis of microscopic polyangiitis. Corticosteroids were continued and the patient required dialysis. The patient's oxygenation improved and he was successfully extubated. The patient was discharged from the hospital on low dose oral corticosteroids and off dialysis.

Discussion: In the United States, the annual incidence of microscopic polyangiitis is 3 cases per one million persons. It is an autoimmune disease consisting of a necrotizing vasculitis of the small vessels, typically arterioles, venules and capillaries. Several organ systems may be affected but the usual cause of death is pulmonary capillaritis and hemorrhage. Less common presentations include rashes (palpable purpura), gastrointestinal bleeding, myocardial infarction, congestive heart failure, and retinal hemorrhages. Microscopic polyangiitis may present indolently, or as a life-threatening emergency. It is difficult to prognosticate which patients will survive.

Conclusion: With adequate treatment, 75% of patients with microscopic polyangiitis will be alive after 5 years, and most patients are on dialysis. The timing of treatment may be the single most important clinical determinant of mortality, and renal failure. Therefore, in patients who present with life-threatening pulmonary-renal syndrome, we advocate early aggressive treatment with antibiotics, plasmapheresis and immunosuppressive drugs.