

# Abstracts

The following abstracts were presented by investigators at the Twenty-First Annual Samuel Bronfman Department of Medicine, Mount Sinai School of Medicine Research Evening on June 8, 2005. 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 11, 2005 and May 25, 2005, respectively.

## Research in Medicine 2005 Mount Sinai School of Medicine

### Basic Science Research

**CD44 Is a Physiological Ligand for E-Selectin on Neutrophils.** J. Chang, Y. Katayama, A. Hidalgo, A. Peired, and P.S. Frenette. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

Selectins and their glycoconjugated ligands are essential for blood neutrophil (PMN) extravasation into inflammatory and infectious sites. However, the identity and contribution of physiological E-selectin ligands (ESLs) on PMNs is largely unknown. This knowledge gap, despite intense research effort, originates in part from the unavailability of inhibitory antibodies, due to the poor immunogenicity of highly glycosylated and conserved ESL epitopes. Mice deficient in P-selectin glycoprotein ligand-1 (PSGL-1), a ligand for all three selectins, exhibit some deficits in E-selectin-mediated rolling but PSGL-1 appears dispensable for E-selectin-mediated PMN extravasation, suggesting a role for other ESLs. A glycoform of CD44 specific to immature progenitor cells was shown to bind to E-selectin *in vitro*. To assess whether CD44 derived from mature myeloid cells could interact with E-selectin, we extracted CD44 from G-CSF-differentiated 32D cells and from mouse PMNs. Immobilized CD44 bound to soluble E-selectin through sialylated,  $\alpha$ 1,3-fucosylated, N-linked glycans. Intravital microscopy analyses of mice deficient in CD44, PSGL-1 or both, revealed that CD44 mediated slow leukocyte rolling on E-selectin in cremaster venules. PMN extravasation in doubly deficient mice, but not either singly deficient mice, was significantly reduced in thioglycollate-induced peritonitis (by 44%,  $p=0.005$ ) or in skin pouches instilled with staphylococcal enterotoxin A (by 77%,  $p=0.006$ ), suggesting that CD44 cooperates with PSGL-1 in mediating E-selectin-dependent PMN extravasation. We also report that CD44 expressed on human neutrophils can bind specifically to E-selectin. Interestingly, neutrophil CD44 purified from a patient with leukocyte adhesion deficiency type II (LADII; which lack selectin ligands) failed to bind E-selectin, but binding of CD44 could be fully restored by incubation of LADII PMNs with  $\alpha$ 1,3-fucosyltransferase VI and GDP-fucose. Thus, our results demonstrate that CD44 is a physiological ligand for E-selectin on mature mouse and human neutrophils.

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**Evidence for Increased Neointima Formation in Podocan Knockout Mice compared to C57/BL6 Wild Type Mice after Arterial Denudating Injury.** R. Hutter\*, L. Huang\*, C. Valdiviezo, J.J. Badimon, and P. Klotman. \*Both authors contributed equally to this study. Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Acute arterial lesion formation is determined by migratory and proliferative cellular events. An important group of extracellular matrix proteins is characterized by small leucine-rich repeat (SLR) sequences and can act as key regulator of cell growth in renal and vascular disease. Podocan is a novel member of the SLR protein family and recently has been shown to be expressed in vascular smooth mus-

cle cells inhibiting cell proliferation *in vitro*. Therefore, we hypothesized that if podocan indeed controls cell growth also *in vivo* mice deficient in podocan might exhibit an increased proliferative response to vascular injury.

**METHODS:** Using a mouse model of arterial injury we examined the effects of podocan genotype on neointimal area and cellularity as well as on the outer arterial wall response to injury. C57/BL6 wild type (WT) mice ( $n=10$ ) and syngeneic C57/BL6 mice either hetero- ( $n=15$ ) or homozygous ( $n=15$ ) for the podocan knockout genotype underwent femoral arterial denudation and were sacrificed at 4 weeks for histopathologic analysis of the injured femoral arterial segment.

**RESULTS:** Mice homozygous for the podocan knockout genotype showed a dramatic and significant increase in neointima area at 4 weeks after arterial injury compared to WT mice ( $11.6 \pm 1.8$  vs.  $4.4 \pm 1.3 \times 10^{-3}$  mm<sup>2</sup>,  $P<0.01$ ). Interestingly, medial area and overall arterial size were not different between the two groups ( $14.5 \pm 0.8$  vs.  $14.8 \pm 2.0 \times 10^{-3}$  mm<sup>2</sup>,  $P=NS$ , and  $50.5 \pm 15.0$  vs.  $53.6 \pm 14.0 \times 10^{-3}$  mm<sup>2</sup>,  $P=NS$ , respectively). Consistently, neointima to media ratio was also strongly increased in podocan knockout mice ( $0.82 \pm 0.12$  vs.  $0.33 \pm 0.10$ ,  $P<0.01$ ). Neointimal cell density per mm<sup>2</sup> did not show a significant difference between podocan knockout and WT mice reflecting increased synthesis of extracellular matrix material by proliferating cells. When comparing mice heterozygous for the podocan knockout genotype to WT mice a similar pattern and trend of data was observed, however it was less pronounced and did not reach the level of statistical significance.

**CONCLUSIONS:** This study represents the first *in vivo* evidence that podocan as a novel member of the SLR protein family is implicated in the regulation of the arterial response to injury process. Mice homozygous for the podocan knockout genotype with complete deficiency in the podocan gene product showed a strong and selective increase in neointima formation with no significant effect on the outer arterial wall architecture. This observation points to a possible specific growth inhibitory/controlling effect of podocan on highly activated intimal smooth muscle cells. However, further studies are necessary to determine the mechanism of podocan-mediated regulation of neointimal growth and to discriminate between local and systemic effects of the podocan knockout genotype.

**VEGF Is a Critical Regulator of Reendothelialization and Neointima Formation in a Mouse Model of Arterial Injury.** R. Hutter, F. Carrick, C. Valdiviezo, C. Wolinsky, J. Rudge, S. Wiegand, V. Fuster, J.J. Badimon, and B.V. Sauter. Cardiovascular Institute, Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Luminal endothelial integrity and rate of re-endothelialization are critical factors in the formation of neointima after arterial injury. VEGF, a potent endothelial mitogen, has been advocated for treating post-angioplasty intimal hyperplasia. A soluble, chimeric VEGF-receptor (VEGF-Trap) has been shown to inhibit endothelial cell proliferation and angiogenesis. To determine the role of VEGF in arterial repair we overexpressed both VEGF and VEGF-Trap in a mouse model of arterial injury.

**METHODS:** Four groups of C57/BL6 mice underwent denuding endothelial injury one day after systemic injection of recombinant ade-

novirus expressing (1) VEGF, (2) VEGF-Trap, (3) VEGF plus VEGF-Trap, or (4) control adenovirus.

**RESULTS:** Circulating transgene levels were significantly elevated 2 and 4 weeks after gene delivery and arterial injury. VEGF treatment significantly accelerated reendothelialization and luminal endothelial cell proliferation as measured by the expression of endothelial Ki-67 (76%  $\pm$  8 vs. 60%  $\pm$  13;  $P < 0.05$ , and 35%  $\pm$  9 vs. 2.3%  $\pm$  0.7;  $P < 0.01$  respectively). This accelerated endothelial repair subsequently resulted in decreased neointima area compared to controls (2.5  $\pm$  1.5 vs. 7.5  $\pm$  2.6  $\times 10^{-3}$  mm<sup>2</sup>,  $P < 0.01$ ). Co-treatment with VEGF and VEGF-Trap eliminated circulating VEGF and completely abrogated the beneficial effect of VEGF on reendothelialization and neointima formation. Interestingly, selective removal of *endogenous* VEGF by VEGF-Trap overexpression alone also led to strong inhibition of reendothelialization at 2 weeks (25%  $\pm$  4.8 vs. 60%  $\pm$  12.6,  $P < 0.01$ ) and increased neointima formation at 4 weeks (17.3  $\pm$  7 vs. 7.5  $\pm$  2.6  $\times 10^{-3}$  mm<sup>2</sup>,  $P < 0.01$ ) compared to controls.

**CONCLUSIONS:** VEGF overexpression accelerated endothelial repair and inhibited neointima formation after arterial injury. Conversely, sequestration of exogenous and/or *endogenous* VEGF by VEGF-Trap inhibited re-endothelialization and dramatically increased neointima size. This emphasizes not only the therapeutic potential of VEGF but also the critical role of physiological VEGF levels and the VEGF pathway in vascular repair *via* maintenance of luminal endothelial integrity.

**Focal Adhesion Kinase (FAK) Abnormalities in Autosomal Recessive Polycystic Kidney Disease (ARPKD).** S. Israeli, K. Amsler, and P.D. Wilson. Department of Medicine, Division of Nephrology, Mount Sinai School of Medicine, New York, NY.

Autosomal Recessive Polycystic Kidney Disease (ARPKD) occurs in 1:20,000 live births. It is characterized by abnormal proliferation of renal epithelial collecting tubule cells, substantial cyst formation and early death (Wilson PD, NEJM 2004; 350:151–164). Mutations in the PKHD1 gene, encoding fibrocystin, cause ARPKD (Ward CJ, et al. Nat Genet 2002; 30:259269). Another form of polycystic kidney disease, Autosomal Dominant Polycystic Kidney Disease (ADPKD), is also characterized by cystic dilation of renal tubules. Renal epithelial cells derived from ADPKD kidneys demonstrate increased extracellular matrix (ECM) adhesion and decreased migration when compared to normal, age-matched, adult human collecting tubule cells.

Correct focal adhesion complex assembly is essential for many cellular functions including ECM attachment, spreading and migration. Binding of cell surface receptors (integrins) to ECM activates integrin clustering and formation of the intracellular focal adhesion complex. Proteins in the focal adhesion complex include focal adhesion kinase (FAK), paxillin, p130CAS, src kinases, talin, vinculin and tensin. Once recruited and activated by phosphorylation at the focal adhesion, the associated focal adhesion proteins recruit and organize actin bundle filaments, further strengthening the focal adhesion complex, increasing cell tension on the ECM, and providing new attachment sites for cell adhesion and motility. Loss of FAK from the focal adhesion complex has been observed in ADPKD cyst lining epithelia (Wilson et al., Lab Invest 1999; 79:1311–1323), suggesting that disruption of downstream signaling events from the focal adhesion impact on the adhesion and motility defects in ADPKD. While the loss of focal adhesion integrity has been established in ADPKD, less is known about focal adhesion complex assembly and downstream signaling in ARPKD.

Preliminary studies have shown increased adhesion to type I collagen and decreased migration in response to growth factor gradient of ARPKD renal collecting duct epithelial cells by comparison to age matched normal human fetal collecting tubule (HFCT) epithelia *in vitro*. Since FAK phosphorylation on tyrosine 397 has been shown to regulate cell adhesion to ECM, PY397- FAK levels were examined in adherent ARPKD versus HFCT cells, as well as total FAK protein content. Both total FAK and FAK tyrosine397 phosphorylation were decreased in ARPKD cells in adherent cells in a time-dependent manner (2–48 hours). Further studies are in progress to determine whether phosphorylation of FAK at other tyrosine and/or serine sites are also altered in ARPKD. Our studies to date, thus show some interesting similarities in adhesion, migration and FAK-phosphorylation defects in ARPKD and ADPKD.

**Effect of Chinese Herbal Formulas on T Cell Responses in Patients with Peanut Allergy or Asthma.** J. Ko, P.J. Busse, L.P. Shek, S. Noone, H.A. Sampson, and X. Li. Pediatric Allergy and Immunology, Mount Sinai School of Medicine, New York, NY.

**RATIONALE:** We previously reported that the “anti-allergy” Chinese herbal formulas ASHMI and FAHF-2 are effective in treating asthma and peanut allergy and in suppressing Th2 responses in murine models. We sought to examine the effect of these two herbal formulas on T-cell responses of patients with allergic asthma or peanut allergy.

**METHODS:** Eight patients with peanut allergy and asthma and six with peanut allergy alone were studied. Peripheral blood mononuclear cells were isolated and cultured with crude peanut extract (CPE, 200  $\mu$ g/ml) with and without herbal formulas (ASHMI for asthmatic patients or FAHF-2 for peanut-allergic patients, 50  $\mu$ g/ml). Proliferative responses and cytokine production were determined by thymidine incorporation and ELISA respectively.

**RESULTS:** Twelve patients with peanut allergy and asthma were studied. Peripheral blood mononuclear cells were isolated and cultured with crude peanut extract (CPE, 200  $\mu$ g/ml) with and without herbal formulas (ASHMI or FAHF-2, 50  $\mu$ g/ml). Proliferative responses and cytokine production were determined by thymidine incorporation and ELISA respectively. For ASHMI, mean thymidine incorporation increased from 500 to 6752 cpm following CPE stimulation and decreased to 5395 cpm with addition of ASHMI. Mean IL-5 production (pg/mL) increased from 77 to 455 following CPE stimulation, decreasing to 212 with ASHMI treatment ( $p < 0.05$ ). Mean IL-13 production (pg/mL) was increased from 1003 to 2564 by CPE, decreasing to 1554 with ASHMI treatment ( $p < 0.05$ ). IL-4 production was undetectable in all samples. Mean IFN- $\gamma$  production (pg/mL) was not suppressed with ASHMI treatment: 55 with medium alone, 707 with peanut extract, and 1098 with ASHMI. T-cell proliferation and cytokine results from peanut allergic patients using FAHF-2 were similar. Cell viabilities in antigen alone and antigen herbal formula-treated cells were not different.

**CONCLUSIONS:** ASHMI and FAHF-2 down-regulated Th2 responses, suggesting that they may have potential benefit to patients with food allergy and asthma.

**KLF6 Tumor Suppressor Has Critical Roles in Vascular, Hematopoietic and Placental Development.** N. Matsumoto. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** KLF6 is a ubiquitously expressed Krüppel-like zinc finger transcription factor identified as a tumor suppressor gene in prostate cancer, colorectal and hepatocellular carcinomas (Tal-Kremer et al., AASLD 2002 #924). *KLF6* is also an immediate early gene that is rapidly upregulated in hepatocytes following partial hepatectomy and in hepatic stellate cells after injury. Its expression is regulated in a tissue-restricted manner during development (Laub et al., Mech Dev 2001). These broad activities yet defined sites of expression suggest a potentially important role of *KLF6* in development. We previously reported the impaired ability of *KLF6*<sup>-/-</sup> ES cells to differentiate into 3 germ layers, resulting in loss of differentiation into an hepatic lineage *in vitro* (Matsumoto et al., AASLD 2003 #267).

The **aim** of this study was to examine the role of KLF6 in mouse embryogenesis.

**MATERIALS AND METHODS:** *KLF6*<sup>+/-</sup> ES cells were generated by homologous recombination through selection with a *KLF6* targeting vector containing the neomycin/lac Z cassette. Chimeric mice were produced by microinjection of targeted ES cell clones into C57BL6 blastocysts, then transferred to pseudopregnant mothers. Chimeric males were mated with C57BL6 females and germline transmission of the mutated allele was verified by Southern blot and PCR analysis of tail DNA from F1 offspring, using two primer pairs amplifying *KLF6* exon2 and neo sequences respectively. Two lines of *KLF6*<sup>+/-</sup> mice were obtained and analyzed.

**RESULTS:** No viable *KLF6*<sup>-/-</sup> mice were recovered among > 300 offspring, and the number of *KLF6*<sup>+/-</sup> mice was ~ 35% less than expected, indicating complete lethality of the *KLF6*<sup>-/-</sup> phenotype and partial lethality of the *KLF6*<sup>+/-</sup> phenotype. *KLF6*<sup>-/-</sup> embryos die between E10.5 to E12.5 and are much smaller, paler, and atretic compared to *KLF6*<sup>+/+</sup> and *KLF6*<sup>+/-</sup> embryos. Although *KLF6*<sup>-/-</sup> embryos had a beating heart at E10.5, vascularization and hematopoietic colony formation assay of *KLF6*<sup>-/-</sup> yolk sacs were severely impaired, suggesting combined defects in vascular development and hematopoiesis. This phenotype implicates a defect in hemangioblasts, thought to be a precursor of

both vascular and hematopoietic tissues. The findings correlate entirely with defects observed during differentiation of *KLF6*<sup>-/-</sup> ES cells (Matsumoto, AASLD 2003 #267). In addition, genetic crosses between *KLF6*<sup>+/+</sup> and *KLF6*<sup>+/-</sup> mice revealed that frequent embryonal deaths in *KLF6*<sup>+/-</sup> mice occurred only when the genotype of the maternal but not paternal mouse was *KLF6*<sup>+/-</sup>. Since *KLF6* is strongly expressed in placenta, this suggests that some maternal factor regulated by *KLF6* may be critical for placentogenesis, which might lead to embryonic deaths of *KLF6*<sup>+/-</sup> and possibly *KLF6*<sup>-/-</sup> mice.

In **conclusion**, these data indicate a broad contribution of *KLF6* to mouse development, with specific roles in morphogenesis, vasculogenesis, hematopoiesis and placentogenesis.

**MMTV-like Particles in Human Breast Cancer.** S.M. Melana, J-D Jiang, S. Dales, J.F. Holland, and B.G.T. Pogo. Mount Sinai School of Medicine, New York, NY, and the Rockefeller University, New York, NY.

We have previously reported sequences homologous to the *env* gene of mouse mammary tumor virus (MMTV) but not to the human endogenous retrovirus in 38% of the 314 human breast cancers studied (Wang et al., Cancer Research 1995; 55:5173). The sequences were absent from other human and tissues and they were expressed in most of the positive breast specimens (Wang et al., Cl. Cancer Research 1998; 4:2565). 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; 61:1754–1759). Structural features of this provirus suggest that it is functional. We have now looked for the presence of viral particles and viral genes in primary cultures of *env* sequence positive tumors. Retroviral particles budding from cells and in particulate fractions from culture media were observed by electron microscopy. Particulate fractions also shown 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 putatively normal breast primary cultures. Taken together, these findings support the identification of a human mammary tumor virus (HMTV) similar to MMTV. Co-cultivation experiments of virus-producing and normal mammary epithelial cells demonstrated transfer of viral sequences and expression of *env* proteins suggesting infectivity.

**Human Alpha Defensin1 Inhibits Influenza Virus Replication by Preventing a PKC-Mediated Entry Event.** M. Salvatore. Mount Sinai School of Medicine, New York, NY.

**INTRODUCTION:** Activation of the innate immunity is the first line of defence of the body against viral infection. In the recent years the complex relationship between the activation of type I interferon system and influenza virus has been extensively studied. Other less studied effectors of the innate immunity are likely to play a role in modulating the body response to viral infection. Alpha-defensins are small, widely distributed antimicrobial peptides present in neutrophil granules that are active against many bacteria, fungi and HIV. It is becoming increasingly clear that defensins play an important role both as effectors of innate immunity and as modulators of adaptive immunity. While their antibacterial activity is attributed to the disruption of cell membranes, their mechanism of action and spectrum of activity against viruses other than HIV is still unclear. We studied the anti-influenza virus activity as well as a mechanism(s) of inhibition  $\alpha$ -defensin-1.

**METHODS:** Recombinant human  $\alpha$ -defensin-1 (HNP1) was obtained from Cell Sciences. Influenza A/WSN/33 virus strain was used to infect MDBK cells (MOI=0.001); titers were measured by plaque assay. For viral protein expression studies, infected cells (MOI=5) were labeled at various intervals with <sup>35</sup>S-Cys-Met. CytoTox 96® assay (Promega) was used to measure cytotoxicity. Activated protein kinase C (PKC) was detected by western blot.

**RESULTS:** Influenza virus replication was inhibited when virus was pre-incubated with HNP1 (25  $\mu$ g/mL) and the inhibitor was present during and after infection (<10<sup>2</sup> vs. 6x10<sup>6</sup>). More importantly, similar inhibitory effect on viral replication was observed when HNP1 was added only after infection (1.7x10<sup>7</sup> vs. 6x10<sup>6</sup>). In contrast, no effect of HNP1 on virus replication was observed when the substance was only present during pre-incubation of virus before infection followed by wash-off and no add-back suggesting that HNP1 blocks influenza virus replication following entry events. The effect of HNP1 was dose-dependent. Time course labeling of protein expression in infected cells

treated with HNP1 showed decreased synthesis of viral (but not cellular) proteins. To ensure that the antiviral effect was not due to general cytotoxicity, cell viability was measured. Treatment of uninfected cells with 10 or 20  $\mu$ g/mL of HNP1 was not associated with cytotoxicity. HNP1 also prevented cytotoxicity by WSN infection in a dose-dependent fashion. HNP1 did not inhibit influenza virus replication in the minireplicon system where the entry events are not necessary for viral infection supporting a block of early event. HNP1 down regulated PKC activation by WSN as demonstrated by a decrease in phosphorylated PKC in HNP1 treated cells.

**CONCLUSIONS:** Our data show that  $\alpha$ -defensin-1 inhibits influenza virus replication following viral entry. The inhibition is dose and time dependent and it is not due to general cytotoxicity.  $\alpha$ -defensin-1 inhibits phosphorylation of PKC which is known to play a role in influenza infection. Since PKC activation is necessary for influenza trafficking in endosomes, HNP1 may block late entry events and inhibit influenza virus replication possibly by inhibiting PKC. The identification of novel effectors of the immune response against influenza virus will provides a better understanding of the host-pathogen interactions and present new strategies for prevention and therapy.

**Significantly Decreased Expression of the Tumor Suppressor KLF6 in 85% of HCCs Contributes to Enhanced Growth and Reduced Differentiation.** S. Kremer-Tal, G. Narla, M. Banck, A.V. Difeo, J-S Lee, E. Zimran, S.S Thorgeirsson, J.A Martignetti, and S.L Friedman. Division of Liver Diseases and Department of Human Genetics, Mount Sinai School of Medicine, New York, NY, Ben Gurion Medical School, Beer-Sheva, Israel and Center for Cancer Research, National Cancer Institute, National Institute of Health, Bethesda, MD.

*KLF6* is a tumor suppressor gene inactivated in a growing number of tumors, including prostate, colon, glioma, lung, head and neck, as well as HCC, suggesting a generalized role in cancer pathogenesis. We have previously established its role in normal hepatocyte growth, whereas it is functionally inactivated in the majority of HCCs by deletion and/or inactivating mutation.

The **aim** of this study was to determine whether *KLF6* expression is decreased in HCC compared to normal livers, and to characterize its effects on cell growth and differentiation in HCC cell lines.

**METHODS:** *KLF6* mRNA levels were quantitated in HCC samples from 39 patients and 10 normal livers by QRT real-time PCR. HepG2 cells stably expressing *KLF6* were established by retroviral infection. Growth was assessed by thymidine incorporation. Growth and differentiation markers were assessed by quantitative RT real-time PCR and western blot.

**RESULTS:** *KLF6* expression was reduced in 33/39 (85%) of patients compared to normal livers, and 25/39 (64%) had levels decreased by more than 50%.

*KLF6* expression levels in HepG2 cells were comparable to those present in patient-derived tumors. Expression levels of *KLF6* RNA and protein were increased to resemble the levels present in normal liver by retroviral infection. Proliferation was reduced by 60% in *KLF6*-expressing cells (p<0.05, n=3), accompanied by reduced expression of cyclin D1 (50%, p<0.0001), c-jun (30%, p<0.05), beta-catenin (35%, p<0.05), TGFbeta1 (30%, p<0.001), and VEGF (50%, p<0.005), and significantly increased expression of E-cadherin (x3.5 fold, p<0.005), albumin (x1.7 fold, p<0.05) and TTR (x3 fold, p<0.005).

**CONCLUSION:** Wild type *KLF6* levels are reduced in the large majority of HCC tumors, and almost 2/3 of tumors had decreases of more than 50% when compared to normal liver. Reconstitution of *KLF6* levels to a "normal" range in the HepG2 cell line resulted in marked growth suppression and increased differentiation. These findings support a role of *KLF6* in growth suppression in normal hepatocytes, and suggest that its downregulation or loss in tumors may contribute to growth and de-differentiation characteristic of HCCs.

**Acid Buffering Gels as Topical Microbicides to Prevent Transmission of Genital Herpes and Other STI.** A.C. Garcia Tuyama. Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** There is an urgent need to develop strategies to prevent HSV transmission. The acidic vaginal milieu (pH ~ 4.0-4.5) is presumed to inactivate STI, but is neutralized by semen (pH 7.2-8.0). The notion that acidic pH provides innate resistance led to the development of acid buffering products as microbicides. However, the extent and

mechanism of anti-HSV activity is not known. These studies were designed to examine the anti-HSV activity of acidic pH, mechanism of activity, and to evaluate *Acidform*, which buffers to pH ~ 4.5, in a murine genital herpes model.

**METHODS:** HSV-2 isolates were mixed with citrate buffer (pH 4.5 and 7.0), neutralized to pH 7.0, inoculated on human cells and plaques counted. Bioadhesive properties preclude testing *Acidform* in culture. Kinetic, binding, and nuclear transport studies were conducted and the impact on glycoproteins evaluated by SDS-PAGE. A murine genital herpes model assessed *Acidform* activity. Controls included placebo gel and PRO 2000, a microbicide in clinical trials that reduces HSV titer by > 4–5-logs *in vitro*. Mice were pretreated with the gels intravaginally, challenged 15 min later with a clinical isolate delivered in PBS or semen and monitored for infection.

**RESULTS:** Exposure of HSV to pH 4.5 followed by neutralization reduced infection by >90%. Kinetic studies indicated that inactivation occurred within 30 min. Pretreatment of HSV-2 with pH 4.5 reduced binding and nuclear transport and modified gB mobility from dimeric to monomeric forms. 22/25 (88%) of mice who received placebo gel developed disease. In contrast, only 5/26 (19%) mice in the *Acidform* group and 0/10 in the PRO 2000 group developed disease. *Acidform* retained activity if mice were challenged with virus delivered in semen. The cytokine response to HSV, characterized by a rapid increase in IL-6 and IFN- $\gamma$  was significantly reduced in mice treated with *Acidform*. *In vitro* studies indicate that PRO 2000 and acidic pH act synergistically to inhibit HSV infection.

**CONCLUSIONS:** These results suggest that acidic pH modifies the viral envelope to prevent binding and entry. *Acidform* offers considerable protection against HSV infection in the murine model and may be an optimal vehicle for formulation of acid-stable topical microbicides to prevent acquisition and transmission of HSV.

**Mouse Embryoid Bodies (EBs) as Surrogate for Human Renal Embryonic Stem (ES) Cells: A Novel Source to Identify Candidate Markers for Renal Stem Cells.** C. Vigneau, K. Polgar, D. Hyink, G. Striker, G. Keller, C. Burrow, and P. Wilson. Mount Sinai School of Medicine, New York, NY.

End-stage renal disease is a major cause of morbidity and mortality and its prevalence is increasing dramatically. The only therapies currently available are renal replacement by transplantation or dialysis. As the supply of donor kidneys is largely inadequate, more than one-half of the patients will remain on the waiting list permanently. Therefore, new therapies to preserve renal function or reverse renal damage are a high priority and utilization of stem cell is an exciting new option. In adult, both bone marrow and kidney niches have been found to contain stem cell. But the major question remains how to identify specifically renal stem cells (RSC) and how to obtain them in sufficient quantity.

Embryonic stem cells (ES) cells are by definition "totipotent" and can generate any cell in any organ. ES can be cultured and maintained undifferentiated in presence of leukemia inhibitory factor (LIF). Without LIF, ES cells differentiate *in vitro*, and generate colonies known as EBs that contain developing cells of many lineages. The renal potential of the ES/EBs system has not been so far investigated. Our hypothesis is that mouse ES cells can give rise to tubular progenitors which are functional and can be integrated in the developing kidney *in vitro* and *in vivo*.

As there is no specific marker for potential RSC, we used a kidney specific combination: *brachyury*, WT-1, Cadherin-11, Pax-2 and Wnt-4. We first determined that after 4 days in culture in serum free conditions, in Activin 10 ng/mL, EBs give rise to cells which express *Brachyury*, WT-1, Cadherin-11, Pax-2 and Wnt-4. Since we used a cell line with GFP knocked in the still functional *brachyury* locus and with  $\beta$ -gal gene expression, these cells can be FACS sorted for *Brachyury* and followed for  $\beta$ -gal expression.

We next tested the functionality of the sorted cells in two different models: *in vitro* injection of cells into embryonic kidney in culture and *in vivo* injection of cells into newborn kidney. Embryonic kidney in culture is a well-defined model to follow development of every renal cells for a few days but not vascular cells. After injection of  $\beta$ -gal RSC, cultured 4 days in Activin 10 ng/mL and FACS sorted for GFP, we found  $\beta$ -gal cells GFP(+) in glomeruli and tubular cells and  $\beta$ -gal cells GFP(-) in the ureteric bud.

Then we injected the same  $\beta$ -gal FACS sorted GFP(+) cells into the left kidney of newborn mice (5 days old). This technique, recently developed in our laboratory, takes advantage of the neogenic zone in newborn mice, and allows the study of renal development *in vivo*. After 5 days after birth, only the tubular cells continue to develop in the

mouse kidney. Two weeks after injection, we sacrificed the mice and stained the kidneys for  $\beta$ -gal. Beta-gal cells have been found in almost all the proximal tubules of the outer cortex of all the left kidneys injected and never in the right kidney of the same animals.

Our data showed for the first time that EBs can give to RSC which can be integrated into the renal parenchyma. Next step will be to focus first on tubular stem cells, to identify more specifically, isolate, and enrich the tubular stem cell population. Same strategy will be also later use to purify podocytes or mesangial stem cells. This characterization will be key to the identification, isolation and expansion of tubular stem cells in adult repositories, such as the bone marrow or the kidney niche.

**Alternative Splicing of the KLF6 Tumor Suppressor Gene During Early Stellate Cell Activation *in Vivo* Is a Proliferative Signal—Resolution of a Paradox.** S. Yea, A. Katz, G. Narla, and S.L. Friedman. Division of Liver Diseases, Mount Sinai School of Medicine, New York, NY.

We previously cloned a novel zinc finger transcription factor, KLF6 (initially termed "Zf9"), which is induced as an immediate-early gene in hepatic stellate cells during liver injury *in vivo* (Ratzju et al., PNAS, 1998). KLF6 was then identified as an anti-proliferative tumor suppressor gene inactivated in several human cancers, and is also a key signal regulating adipogenesis through trans-repression of Dlk-1, an important inhibitor of this differentiation event. The finding that KLF6 is growth suppressive gene, yet rapidly induced when stellate cells undergo a proliferative burst, represented a paradox that has defied explanation. More recently, however, alternative splicing of KLF6 has been identified in rodents and humans, with generation of shorter, dominant negative isoforms that lack all or part of the DNA binding domain. These isoforms are increased relative to wt KLF6 in HCC, prostate and ovarian cancers, but their role in non-malignant tissue responses is not known. The aims of our study were: (1) to determine if early stellate cell activation leads to increased alternative splicing of KLF6; (2) to assess the biologic activity of KLF6 splice forms in cultured cells and (3) to define specific stimuli that regulate KLF6 alternative splicing.

**METHODS:** We assessed KLF6 alternative splicing by PCR and Western blot in mouse stellate cells isolated at intervals following a single dose of CCl<sub>4</sub>. The response of cultured stellate cells to key fibrogenic stimuli *in vivo* were assessed in a culture model.

**RESULTS:** Alternative splicing of KLF6 increases during stellate cell activation *in vivo* and persists in activated stellate cells in culture. These splice proteins accumulate in the cytoplasm, have prolonged half-lives, abrogate wild type function as true dominant negatives that block induction/repression of wt KLF6 targets, and additionally lead to gain of function of transcriptional targets not ordinarily regulated by KLF6. KLF6 splicing is also induced in stellate cells by oxidant stress, and appear to be regulated by Ras activity. Using a splice-specific monoclonal antibody, these isoforms appear to be selectively expressed at a low level in stellate cells even in normal human liver.

**CONCLUSIONS:** Generation of alternative splice forms of KLF6 during stellate cell activation *in vivo* and in response to fibrogenic signals explains the paradox of its induction during the onset of a proliferative response of the cell type. Independent of its tumor suppressor activity, KLF6 appears to be an important signal regulating cellular differentiation, in part through the titration of full length vs. alternative splice forms. Alternative splicing of this transcription factor represents a novel mode of regulating gene expression not previously described in hepatic stellate cell biology.

## Clinical Research

**Tuberculous Dactylitis in a 46-Year-Old Male with HIV.** S. Agarwal and D. Caplivski. Mount Sinai School of Medicine, New York, NY.

Extrapulmonary manifestations of tuberculosis have become increasingly important in the era of HIV/AIDS. We describe a case of tuberculosis (TB) dactylitis in a patient with AIDS who originated from the Ivory Coast. The diagnosis was established by direct visualization of acid fast bacilli on bone biopsy of the proximal phalanx. Tuberculosis should be considered in patients with unusual skeletal lesions, especially when an immunosuppressive condition is present. Ziehl-Neelsen

staining and culture of tissue obtained via surgical biopsy offer the most direct approach to diagnosis.

**Anger Justification and Blood Pressure: A Different Story for Men and Women over the Life-Span.** N. Rieckmann<sup>1</sup>, D. Abraham<sup>1</sup> and K.W. Davidson<sup>2</sup>. <sup>1</sup>Medicine, Mount Sinai School of Medicine, New York, NY, and <sup>2</sup>Medicine, Columbia University, New York, NY.

A constructive way of discussing one's anger (CABV) has been shown to be associated with lower resting systolic blood pressure (SBP). We hypothesized that overtly justifying one's anger (e.g., being determined to show one's own standpoint) would have an adverse effect on SBP.

BP medication-free men (n=688; age 18–90 years) and women (n=604; age 18–93 years) from a population-based, random sample underwent a stressful interview, which was rated for Anger Justification (alpha=0.88). An average resting SBP score was computed from 4 readings (alpha=0.95).

Surprisingly, Anger Justification was positively associated with CABV in both men (r=.22, p<0.01) and women (r=.24, p<0.01), and negatively associated with SBP for women only (r=-.12; p<0.01). Regression analyses were conducted; age, body mass index, parental history of MI, weekly alcohol intake, current smoking status, weekly physical activity, and education were entered first, and Anger Justification second. To examine age trends, the interaction term of age and Anger Justification was entered third. In men, Anger Justification was a significant predictor with only 1% of variance explained (p<0.05), but controlling for CABV rendered it insignificant. In women, no additional variance was explained by Anger Justification, but the interaction was significant (p<0.05), and remained significant when controlling for other psychosocial measures (CABV, anxiety, depression, hostility). Post-hoc analyses revealed that only in women over 65 years of age did Anger Justification significantly predict lower SBP (5% of variance), controlling for standard risk factors.

Thus, Anger Justification seems to have a strong beneficial effect for older women, but not for men at any age. Possible cohort, developmental, and methodological explanations for this benefit will be discussed.

**Insulin Initiation in Poorly Controlled Diabetics.** S.J. Adamcik. Mount Sinai School of Medicine, New York, NY.

**CONTEXT:** The decision to initiate insulin therapy in patients with type 2 diabetes is influenced by many factors including measured indices of glycemic control, presence of diabetes related comorbidities, and provider/patient preferences.

**OBJECTIVE:** To determine if the presence of a specific macrovascular event or outcome in a poorly controlled diabetic patient correlates with an Internal Medicine resident's decision to initiate insulin therapy.

**DESIGN, SETTING, POPULATION:** The Internal Medicine Associates (IMA) is the continuity clinic for the Mount Sinai Internal Medicine residency training program and serves a population of patients with a high prevalence of type 2 diabetes—the East Harlem section of New York City. The medical record of 500 IMA patients with type 2 diabetes will be reviewed and information regarding level of glycemic control, presence of macrovascular disease and pharmacologic diabetic regimen will be recorded and analyzed.

**MAIN OUTCOME MEASURE:** Rates of insulin initiation in type 2 diabetic patients with documented evidence of macrovascular disease.

**HYPOTHESIS:** In Type II diabetic patients with laboratory evidence of poor glycemic control (HgbA1c levels >7.5), Internal Medicine residents at a large inner city clinic are more likely to initiate insulin therapy in those patients with documented evidence of macrovascular disease as compared to those with no evidence of macrovascular disease.

**CONCLUSIONS:** (Preliminary-ongoing data analysis). Poorly controlled patients with documented evidence of macrovascular disease had a statistically significant greater incidence of insulin use.

**Utility of CACS in Assessing Cardiovascular Risk in a Lipid Specialist's Practice.** A. Aronovitz. Mount Sinai School of Medicine, New York, NY.

Coronary calcium scores have been proposed as a method to predict cardiac risk. It has been shown that the calcium score on electron beam com-

puterized tomography (EBCT) correlate with plaque burden. As a result, it has been suggested that EBCT may be used as a screening tool to identify patients with arteriosclerosis, and therefore, at greater risk for CHD. Initial studies have supported this theory, and in fact, the ATP-III guidelines recommend EBCT for patients at intermediate cardiac risk. We would like to perform a retrospective analysis on 170 patients at low to intermediate cardiac risk who have had EBCT between 1998–2004. The study will assess whether coronary calcium scores provide added value to the Framingham risk score (FRS) alone when evaluating cardiac risk.

**Cerebrospinal Fluid Pleocytosis in HAART-Era AIDS Cohort: Clinical Correlations.** A. Borad, L. Estanislao, S. Wallenstein, S. Hossain, and S. Morgello. Mount Sinai School of Medicine, New York, NY.

**BACKGROUND/OBJECTIVES:** Cerebrospinal fluid (CSF) pleocytosis is known to occur in individuals with HIV infection. We determine the presence of CSF pleocytosis, and its relation to antiretroviral usage, as well as its impact on the neuropsychologic performance and neurologic status of subjects enrolled in Manhattan HIV Brain Bank, a prospective study of an advanced AIDS cohort.

**METHODS:** Data from subjects who underwent serial lumbar puncture (LPs), clinical, neuropsychologic (NPE) and neurologic examination (NE) every 6 months from January 1999 to October 2004 were obtained.

**RESULTS:** There were 107 subjects (30 females, 77 males) of whom 32 (30%) had at least one episode of cerebrospinal fluid (CSF) lymphocytic pleocytosis (WBC  $\geq 6$  c/uL). Subjects with opportunistic brain infections were excluded. There were a total of 365 LPs performed. The presence of CSF pleocytosis correlated with the absence of antiretroviral (ARV) use at the time of the LP (21 CSF pleocytosis off ARV vs. 251 without CSF pleocytosis on ARV) (Fisher's exact test 0.001).

**CONCLUSION:** HIV-infected individuals on antiretrovirals are less likely to have CSF pleocytosis.

**Geriatric Ambulatory Medical Education for Internal Medicine (IM) Residents: The Need for Faculty Development.** C. Chang, E. Widera, L. Fry, S. Bradley, D. Thomas, E. Chai, and R.M. Leipzig. Supported by: Departments of Geriatrics and Internal Medicine, Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** National surveys indicate a need for additional training in geriatrics during IM residencies. Though MSSM IM residents receive an excellent introduction to inpatient geriatrics during their ACE Unit and Geriatric Consult Service rotations, no formal ambulatory geriatric curriculum exists.

**OBJECTIVE:** To identify IM resident and precepting faculty needs for formal education in geriatric ambulatory care.

**METHOD:** A Needs Assessment Survey was developed and administered to all IM residents and precepting faculty in June 2004. Baseline personal and education demographics were obtained. Respondents were asked to rate 19 geriatric ambulatory care topics using a 5-point Likert-type scale in terms of: (1) importance for internists to learn during residency, (2) actual training during ambulatory block, continuity clinic and house calls, (3) adequacy of training and (4) perceived capacity of IM faculty to teach geriatric ambulatory topics.

**RESULTS:** A total of 50 residents (45.4%) and 27 faculty (65.9%) completed the survey. Both faculty and residents felt that all 19 geriatric ambulatory topics were important (range of means 3.766–4.633, where 0=least and 5=most important). However, only certain topics were actually and adequately taught. These topics were mostly disease states common in the elderly (e.g., CAD and DM) rather than geriatric syndromes or functional assessment. Both faculty and house staff felt that these topics were important and that the faculty were capable of teaching them. Because faculty felt less comfortable teaching geriatric syndromes and functional assessments, these topics were taught less frequently or adequately, and were generally ranked as less important for internists to learn.

**CONCLUSION:** Though IM residents and faculty ranked the 19 geriatric ambulatory topics as need-to-know, only topics that faculty felt they had good capacity to teach were actually and adequately taught and felt, by both groups, as important for internists to learn—the result is that residents do not believe it is important to learn topics which the faculty do not feel competent to teach. For house staff to graduate competent in caring for ambulatory geriatric patients, precepting IM faculty will need to learn the content and how to teach these other important geriatric ambulatory care topics.

**Searching for Cardiac Sarcoidosis.** A.S. Teirstein<sup>1</sup>, Z.B. Frankel<sup>2</sup>, A.J. Einstein<sup>2</sup>, D. Mehta<sup>2</sup>, M.L. Padilla<sup>1</sup>, and M.Iannuzzi<sup>1</sup>. <sup>1</sup>Division of Pulmonary, Critical Care and Sleep Medicine, Department of Medicine, and <sup>2</sup>Department of Cardiology, Mount Sinai School of Medicine, New York, NY.

The following abstract has been submitted to the WASOG conference.

In the United States, clinical cardiac sarcoidosis is reported in approximately 5% of patients, and at autopsy in 25%. Ventricular arrhythmias and myocardial failure are the common presenting clinical manifestations. Unfortunately, in many patients cardiac disease is occult and sudden death is the initial presentation. All patients with sarcoidosis are at risk for cardiac involvement. A variety of cardiac studies have been employed in the diagnosis. The requisite minimal tests to screen patients and the studies required to follow patients have not been clearly delineated. Indications for implantation of electrical devices are not entirely clear. Recently, PET scans and MRI scans have exhibited value in the diagnosis and follow-up of cardiac sarcoidosis. At the Mount Sinai Medical Center, NY, 100 patients with biopsy proven sarcoidosis have been enrolled in a study in an attempt to generate an algorithm for the proper diagnosis and treatment of cardiac sarcoidosis, and the indications for implantation of cardioverter defibrillators. All 100 were screened with complete history, physical examination, standard chest radiography, pulmonary function studies, blood tests, EKG, Holter monitor and echocardiograms. Twenty-six patients with abnormal cardiologic screen were referred for PET scan and MRI scans. Demonstration of cardiac arrhythmias prompted placement of cardioverter devices. MRI and PET scans demonstrated sarcoïdal cardiac abnormalities, often affecting medical therapy.

**The Incidence of Protease Inhibitor-Associated Mutations in Patients Taking Atazanavir.** D. Caplivski<sup>1</sup>, C. Salama<sup>1</sup>, and D. Caplivski<sup>2</sup>. <sup>1</sup>Mount Sinai School of Medicine, Elmhurst Hospital Center, Elmhurst, NY and <sup>2</sup>Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Atazanavir is a new protease inhibitor (PI) used in HIV treatment. The signature protease gene mutation associated with atazanavir resistance is I50L. There is limited data about other mutations associated with the clinical use of atazanavir.

**METHODS:** The Elmhurst Clinic Database consists of 1240 genotype tests (GT) from 743 patients at the Elmhurst Hospital Immunology Clinic. Forty-three patients had undergone GT while taking atazanavir and were divided into 3 groups: 1. Patients with no prior PI experience (n=10). Six used concomitant ritonavir, 4 did not. 2. Patients with PI experience, but without significant PI-associated mutations (n=15). Eleven used concomitant ritonavir, 4 did not. 3. Patients with previous PI therapy and significant PI mutations (n=15). Fourteen used concomitant ritonavir, 1 did not.

**RESULTS:** Group 1: No significant new PI mutations were detected. New polymorphisms detected included L63P, V77I. Mean viral load at GT was log 4.5. Group 2: One patient who had previously taken nelfinavir manifested a D30N on GT. No other significant mutations were detected. New polymorphisms detected included M36I, K45R, G73S, L63P, I93L. Mean viral load at time of GT was log 4.9. Group 3: Significant pre-existent mutations seen in this group included 1 with D30N, 9 with M46I, 3 with G48V, 1 with I50V, 7 with I54V/T, 8 with V82A/F, and 11 with L90M. After atazanavir use one patient manifested a V82A/S and an L90M. This patient was taking atazanavir with agenerase and norvir, but no nucleoside backbone. No other significant mutations developed and no patients developed the I50L or N88S mutations. New polymorphisms detected included K20I/R, F53L, G73S, T74A/S, I93L. Mean viral load at time of GT was log 4.5. The mean duration of therapy prior to GT was 5.13 months.

**CONCLUSIONS AND SUMMARY:** Patients taking atazanavir are at low risk for significant new PI-associated mutations early during virologic failure.

**Genes and Pathways Involved in the Molecular Pathogenesis of Hepatocellular Carcinoma in HCV-Cirrhotic Patients.** Y-B Chen, E. Wurnbach, S. Roayaie, I. Fiel, M. Schwartz, S. Thung, G. Khitrov, W. Zhang, V. Mazzaferro, J. Bruix, E. Bottinger, S. Waxman, S. Friedman, and J.M. Llovet. Mount Sinai Medical Center, New York, NY, and Istituto Nazionale di Tumori, Milan, Italy, Hospital Clinic, Barcelona, Spain.

The molecular pathogenesis of hepatocellular carcinoma (HCC) is complex, and insufficient data are available on the key genes involved

in the initiation and progression of liver carcinogenesis. To characterize the gene expression profiles of pre-neoplastic lesions and HCC in cirrhotic patients due to hepatitis C virus (HCV) infection, we assessed the expression patterns of 52 genes that have previously been associated with liver carcinogenesis in 78 samples from 52 patients by quantitative Real-Time RT-PCR. The samples represented all stages of the stepwise progression process with emphasis on the transition from pre-neoplastic lesions to HCC: normal tissue (10), cirrhotic tissue (10), low grade dysplastic nodules (10), high grade dysplastic nodules (8) and four stages of cancer from very early HCC to metastatic tumors/gross vascular invasion (40). Specific mRNAs were quantified by using probe/primer sets from *Taqman Gene Expression Assays* and altered key genes were further confirmed using additional primers by SYBR Green method.

We identified genes that were significantly up-regulated across the spectrum of the hepatic carcinogenic process such as TERT, STK6, Glypican-3, survivin and TOP2A, as well as others that were down-regulated such as XLKD1, E-cadherin, IGFBP3, and HGF [ANOVA, p=0.001 for all]. Some other gene alterations observed were more stage-specific. Dysplastic nodules already harbored significant de-regulated genes compared with cirrhotic or normal liver tissue. Logistic regression analysis identified LYVE1 (8-fold down regulation in HCC, p=0.0001), E-cadherin (2.5-fold down-regulation in HCC, p=0.001) and survivin (2.3-fold up-regulation in HCC, p=0.001) as the most informative genes to discriminate dysplasia from early cancer. In addition, we found a 3-gene model that correlated with the metastases of HCC. Our results indicate a common activation of Wnt signaling pathway in early HCC, and potential involvement of EGF receptor tyrosine kinase activated pathways in a sub-population of HCCs: EGF showed a 5-fold up-regulation in 17/40 HCCs (vs. 0/28 cirrhosis and pre-neoplastic nodules, p=0.0001), and SOCS1 was significantly down-regulated in 10/40 HCCs in comparison with 0/10 cirrhotic tissue (p=0.01).

These data provide a comprehensive profile of key changes in gene expression and signaling pathways associated with the stepwise progression of HCC due to HCV infection. Further studies with DNA microarrays and biochemical methods are underway to complement this approach.

**Predictors of Death among a Homebound Admission Cohort of a Home-Based Primary Care Program.** L DeCherrie<sup>1</sup>, J Penrod<sup>1,3</sup>, K Ornstein<sup>2</sup>, T Hochman<sup>3</sup>, and J Boal<sup>2</sup>. Departments of <sup>1</sup>Geriatrics and <sup>2</sup>Medicine, Mount Sinai School of Medicine, New York, NY, and <sup>3</sup>GRECC, Bronx VA Medical Center, Bronx, NY.

The number of frail, homebound people unable to get to the doctor is increasing. Homebound patients, who tend to have multiple medical problems and poor functioning, often are unable to get primary care. Programs where physicians make home visits are increasing. It is likely that home-based primary care patients represent a vulnerable cohort, but little is known about their overall prognosis.

**OBJECTIVE:** To examine risk factors for death in homebound patients in a home-based primary care program (HBPCP).

**METHODS:** Retrospective chart review of new enrollees in a HBPCP (n=262) between 1/03 and 6/04, followed until death (n=35), discharge (n=26), or study termination (11/04). A Cox proportional hazards model was used to examine the relationships among demographic and clinical characteristics at admission and mortality.

**RESULTS:** The sample included 193 (80%) women, 86% ≥65 years (25–102 yrs), 24% black, 23% Latino and 50% white, 59% had dementia, 6% had pressure ulcers, mean Charlson co-morbidity score 2.25, and 66% were dependent in ≥ 4ADL's. The mortality rate was 10.4% and 16.3% at 6 and 12 months after admission. An increased risk of mortality was associated with being older (HR, 1.05, 95%CI, 1.01–1.10), having a high school degree (HR, 3.69, 95%CI, 1.03–13.25), living with family compared to a paid caregiver (HR, 3.23, 95%CI, 1.15–9.09), having more comorbidities (HR, 1.46, 95%CI, 1.16–1.85), pressure ulcers (HR, 7.56, 95%CI, 1.86–30.71), and ≥6 prescription medications (HR, 11.01, 95%CI, 2.38–51.03), being dependent in all ADL's (HR, 14.22, 95%CI, 1.56–129.68), and having a home attendant ≥85 hours per week (HR, 3.87, 95%CI, 0.96–15.58). The risk of mortality was lower for patients with dementia (HR, 0.25, 95%CI, 0.10–0.65) and independent in 2–3 IADL's (HR, 0.16, 95%CI, 0.23–2.09). Gender, ethnicity, Medicaid, depression, incontinence, peg tube, falls, recent hospitalization, and caregiver stress were unrelated to mortality risk.

**CONCLUSIONS:** Homebound people, even those connected to a HBPCP, have a high risk of mortality, similar to the rate found in a community based long-term care program. Mortality was higher for pa-

tients with more functional impairments and multiple illnesses, including pressure ulcers at enrollment. These findings highlight the vulnerability of this cohort and should be considered by clinicians who will care for this growing population.

**Effect of Novel Combination Therapies in the Treatment of Chronic Hepatitis B.** A. Ala, N. Karanth, T. Foster, and D. Dieterich. Division of Liver Diseases, Mount Sinai School of Medicine, New York, NY.

**INTRODUCTION:** Interferon, adefovir, and 3TC (lamivudine), are approved for the treatment of hepatitis B (HBV), FTC (emtricitabine) and tenofovir (TDF) are approved for HIV but exhibit significant HBV activity. Hitherto, there has been little data on the use of combining these agents in the treatment of chronic hepatitis B. Utilizing two (or more) nucleoside analogues, as used in the treatment of HIV, is theoretically sound. It should maximise viral suppression, thereby reducing the chance that resistance will develop. We used some of these drugs in combination to treat naïve HIV seronegative patients with chronic HBV.

**AIMS:** In this pilot study we report our overall experience with combination therapy in mono-infected patients. Our study was to assess the effect of combined drug regimens on viral load and seroconversion in the treatment of patients with chronic HBV.

**METHODS:** Fifteen patients (age 30–54, 11 males and 4 females) with chronic HBV were followed from 6 months–9 years. They were divided into the following treatment regimens: Group 1 (n=4): 3TC and/or 3TC+famciclovir followed by addition of TDF or increasing doses of 3TC to 300mg. Group 2 (n= 6): Adefovir followed by supplementation of 3TC (300mg) or TDF. Group 3 (n=5): any other monotherapies (e.g., Interferon, Entecovir, FTC) followed by combination therapy (including 3TC 300mg and/or TDF).

**RESULTS:** Six of the 7 patients who were given increased doses of 3TC (300mg) were able to maintain sustained viral suppression; prior treatments on monotherapy had yielded at best only refractory improvements in viral suppression until that point. Of these, two were found to have seroconverted after 4 and 20 weeks respectively. Three precore mutants were part of this sub-cohort, one of whom was the only failure of therapy in this study. All patients (total of six, including 2 precore mutants) who were treated with TDF as salvage therapy showed sustained viral suppression. There was no evidence of seroconversion in this subset of patients. Two patients originally included in the study were lost to follow up.

**CONCLUSION:** Combination therapies may be an effective treatment in those patients with chronic HBV who fail to respond to conventional management. Our experience shows TDF as a viable salvage therapy for suboptimal response to adefovir. Furthermore, the addition of 3TC at increased doses (300mg vs. 150mg) proved to be effective in the suppression of HBV DNA levels, from 12 weeks up to greater than 2 years after implementation of therapy. Precore mutants benefit from 3TC supplementation to adefovir. Clearly a larger cohort of patients is required to assess combination future chronic hepatitis B therapy.

**Statin Therapy and Acute Coronary Syndrome: The Common Practice at Mount Sinai.** T. Pilar and P. Stevens-Cohen. Mount Sinai School of Medicine, New York, NY.

Recent data has emerged in the field of cardiology suggesting that maximum dose lipid lowering agents have decreased mortality and morbidity in patients with acute coronary syndrome (ACS). Many of the studies used maximum therapy regardless of baseline lipid profiles. This data has changed the way we manage ACS at Mount Sinai. Traditionally, such patients were started on lipid lowering agents on a dose that was largely determined by their lipid profile. These patients would be followed by their primary care physicians and cardiologists, who would titrate lipid-lowering agents to a goal LDL <100. Currently, patients with ACS are being discharged on maximum therapy regardless of their lipid profile making us redefine the role of lipid profiling in ACS. (There is also data stating that lipid levels are not accurate in the setting of ACS due to its highly inflammatory state).

While there is data supporting this treatment, there is no current standard of care regarding the duration of therapy. Furthermore, if patients are being started on intense cholesterol lowering medicine regardless of initial lipid profile, how are these medicines adjusted on an out-patient basis? Has the old standard of LDL <100 changed? The side effect profile of cholesterol agents is well defined. Since we are start-

ing to use higher dose therapy, we expect to see a higher incidence of myositis and liver function abnormalities.

We conducted a survey of medicine housestaff, attendings, cardiology fellows and attendings to see if there is a standard of care at Mount Sinai. We proposed that housestaff and cardiologists rotating through the CCU, would be more likely to discharge patients home on high dose statin therapy, regardless of initial lipid profile. There is no standard of time regarding the length of treatment. The purpose of the second half of the questionnaire was to survey how long patients were being treated with statins and how the medications were being titrated.

**Impact of Ambulatory BP Monitoring on Living Kidney Donation.** E. Herman. Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Living kidney donation is becoming increasingly important in kidney transplantation, due to improved graft and patient survival in recipients from living donors versus cadaveric donors, as well as avoidance of a lengthy waiting list and the possibility of pre-emptive transplant. Most transplant centers exclude hypertensives from kidney donation due to concerns of worsened renal and BP outcomes. Ambulatory BP monitoring (ABPM) measures BP multiple times over a 24-hour day in a patient's usual setting. ABP is more closely associated with evidence of target-organ damage and is a better predictor of cardiovascular events than clinic BP (CBP). ABP allows identification of white-coat hypertension (WCH), those with elevated CBP but normal ABP; these patients have been shown to have risks of cardiovascular events similar to patients with sustained normotension. ABP also identifies "masked hypertension" (MH), when CBP is normal but ABP is elevated; these patients have target-organ damage and rates of cardiovascular events similar to sustained hypertensives.

**METHODS:** Potential living kidney donors undergoing initial nephrology evaluation at the Recanati/Miller Transplantation Institute were invited to participate. Subjects wore a Spacelabs 90217 ABPM for 24 hours, during which time the monitor obtained BP readings every 20–30 minutes. Subjects with fewer than 10 daytime and 4 nighttime readings were excluded from the study. CBP was compared to mean 24-hour ABP for each subject. Hypertension by CBP was defined as  $\geq 140/90$ , and hypertension by ABP was defined as  $\geq 135/85$ .

**RESULTS:** A total of 70 potential donors enrolled in the study. Demographic information is listed in Table 1.

Categorization as normotensive or hypertensive by CBP and ABP is shown in Table 2. 23 subjects were hypertensive by CBP. Of these, 18 (78%) were normotensive by ABP, giving a total prevalence of WCH of 26%. These subjects were medically cleared for donation. 2 subjects who were normotensive by CBP were found to be hypertensive by ABP, giving a prevalence of MH of 3%. These subjects were excluded from donation.

Table 1

	Male/Female	White	Black	Hispanic	Other race/ ethnicity
N	27/43	20	20	24	6
%	39/61	29	29	34	9

Table 2

		Ambulatory BP		
		Normotensive	Hypertensive	
Clinic	Normotensive	45	2	47
BP	Hypertensive	18	5	23
		63	7	70

**CONCLUSION:** There is a high-incidence of WCH in potential living kidney donors. The use of ABPM in initial evaluation of potential donors may expand the potential donor pool, while ensuring protection of potential donors by identifying those with MH.

**Verification of the Efficacy of an Assay for Establishing Microbicide Use in a Pilot Clinical Study.** A. Kasowitz<sup>1</sup>, K. Hogarty<sup>1</sup>, C. Goldberg<sup>2</sup>, S. Patel<sup>1</sup>, B. Herold<sup>2</sup>, and M. Keller<sup>1</sup>. Divisions of <sup>1</sup>Medicine-ID and <sup>2</sup>Pediatric-ID. Mount Sinai School of Medicine, New York, NY.

**OBJECTIVES:** To evaluate an accurate, rapid, and inexpensive method for verifying participant use of single-use intravaginal plastic applicators in a pilot clinical microbicide study.

**STUDY DESIGN:** In a published study, a trypan blue assay was developed to establish whether Microlox-type microbicide applicators had been exposed to the vagina. To verify this assay, single-use intravaginal plastic applicators were collected after use from 16 sexually abstinent, healthy women enrolled in a once-daily, placebo-controlled 14-day microbicide trial designed to evaluate safety. Participants inserted the first dose of 0.5% PRO 2000/5 Gel or Placebo Gel under the observation of the study clinician and were instructed to insert one dose each night at the hour of sleep for 13 subsequent days. Subjects were given a study diary to record time and date of gel use. Used applicators were placed into individual plastic bags and returned to the study staff at subsequent study visits. Each applicator was dyed with 0.4% trypan blue, air-dried for 5 minutes and rinsed gently in distilled H<sub>2</sub>O. The first applicator used served as the positive control, and several unused applicators were dyed in the same fashion to serve as negative controls. Two blinded observers rated the applicators as used or unused and these results were compared to the subjects' self-reports.

**RESULTS:** In 99% of cases, observers' findings correlated with the participants' self-reports; used applicators were easily distinguished from unused applicators. In a subset of cases, the examiners were able to distinguish between applicators that had been used intravaginally and applicators that had been filled with study gel and emptied *ex vivo*.

**CONCLUSION:** Trypan blue staining of single-use intravaginal plastic applicators is accurate, rapid, inexpensive, and correlated well with participant self-report in this study. This simple method could prove useful in interpreting data from future large-scale microbicide efficacy studies.

**Dosing of Radiocontrast for Interventional AV Fistula Salvage Procedures in Stage 4 Chronic Kidney Disease Patients.** K. Kian<sup>1</sup>, C.M. Wyatt<sup>1</sup>, D. Schon<sup>2</sup>, J. Packer<sup>2</sup>, J.A. Vassalotti<sup>1</sup>, and R. Mishler<sup>2</sup>. <sup>1</sup>Department of Nephrology, Mount Sinai Medical Center, New York, NY, and <sup>2</sup>Arizona Kidney Disease and Hypertension Ambulatory Surgery Center, Phoenix, AZ.

**BACKGROUND:** The Dialysis Outcomes Quality Initiative emphasizes on increasing arteriovenous fistula prevalence, by promoting referral for fistula creation in patients with stage 4 chronic kidney disease (CKD). The aim of early fistula creation is to provide an optimal access for initiation of dialysis, thus avoiding central venous catheter use. The endovascular management of non-maturing fistulas is more complicated in these patients, where the expected benefit of catheter avoidance must be weighed against the risk of contrast induced nephropathy (CIN). This study describes the experience of an interventional nephrology center in performing endovascular procedures in patients with stage 4 CKD.

**METHODS:** All consecutive endovascular procedures performed over a two-year period in patients with stage 4 CKD and non-maturing access were identified. Data collected included the type of procedure performed, amount of contrast used per procedure, pre, 2-day and 7-day creatinine, need for acute dialysis and the type of access used to initiate dialysis.

**RESULTS:** A total of 65 procedures were performed in 34 patients. A mean dose of 7.8 mL of contrast was used per procedure. The incidence of CIN (25% increase in serum creatinine) was 4% at two days and 4.6% at one week. All values returned to baseline within two weeks, and no patient required acute dialysis. Among the 33 patients with fistulas, 15 had started dialysis using the fistula (45%), 13 (39%) remained in CKD, and 5 (15%) patients required a catheter at the initiation of dialysis.

**CONCLUSION:** This study demonstrates that in patients with advanced CKD, fistulas can successfully be salvaged with a low CIN incidence using very small contrast volumes.

**Achieving Optimal Treatment Goals in Patients with Stage III Chronic Kidney Disease.** V. Konduri<sup>1</sup>, C. Wyatt<sup>1,2</sup>, J. Eng<sup>1</sup>, and R. Rohatgi<sup>1,2</sup>. <sup>1</sup>Department of Medicine, Bronx Veterans Affairs Medical Center, Bronx, NY, and <sup>2</sup>Division of Nephrology, Department of Medicine, Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Chronic kidney disease (CKD) is defined by the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines as a glomerular filtration rate (GFR) < 60 mL/min/1.73m<sup>2</sup> or the presence of microscopic/macrospecific albuminuria. Although CKD is estimated to affect more than 10% of adults in the United States, it often goes unrecognized because serum creatinine is an unreliable marker of GFR. The K/DOQI guidelines advocate the use of the Modification of Diet in Renal Disease estimation of GFR (MDRD eGFR) to identify and stage patients with CKD; however, the effect of routine GFR estimation on clinical practice has not been evaluated.

**HYPOTHESIS:** We hypothesize that routine reporting of MDRD eGFR will increase ACE inhibitor utilization, blood pressure control, and measurement of urine protein.

**METHODS:** We plan to compare clinical practice patterns before and after institution of routine MDRD eGFR reporting in the Bronx VA primary care population. To minimize the effects of evolving practice guidelines, we will compare the periods immediately before and after implementation of eGFR reporting. The data presented in this abstract reflect the pre-eGFR reported group where the baseline practice patterns were measured. All individuals with a measured serum creatinine between July 1, 2003 and June 30, 2004 were included in this study. Of these patients the following data was extracted from the chart: age, race, gender, ace inhibitor (ACEi) or angiotensin receptor blocker (ARB) use, urinalysis, last recorded blood pressure and history of diabetes. The abbreviated MDRD calculation was used to determine eGFR.

**RESULTS:** 15,155 patients of the 21,285 Bronx VA patients had a measured serum creatinine and, of these individuals, 2,564 (16.9%) patients had an eGFR  $\leq$  59 mL/min/1.73m<sup>2</sup>. 14.5% (2,201/15,155) of patients had stage III CKD (30–59 mL/min/1.73m<sup>2</sup>) with an average age of 75.0 $\pm$ 9.8 years old and serum creatinine of 1.58 $\pm$ 0.29 mg/dL. Approximately 30% (661/2201) of stage III CKD patients were diabetics. Since ACEi/ARBs are known to decrease the progression of diabetic nephropathy and this population had a high prevalence of diabetes, we stratified stage III CKD patients into diabetics and non-diabetics under the hypothesis that diabetes is a much more potent marker for ACEi/ARB utilization than CKD itself. We then evaluated care in both groups by studying ACEi/ARB utilization, achievement of blood pressure control (<130/80) and urinalysis testing. Only 47.7% (735/1540) of non-diabetics vs 85.3% (564/661) of diabetics were prescribed ACEi/ARBs. Similarly, urinalyses were underutilized in non diabetics (47.8%; 736/1540) vs. diabetics (74.6%; 493/661) with CKD. However, blood pressure control of <130/80 was achieved in 48.1% (741/1540) of non-diabetics vs. 35.2% (233/661) of diabetics with CKD.

**CONCLUSIONS:** ACEi/ARB and urinalysis utilization amongst diabetic patients is greater than in non-diabetics with stage III CKD; however, achievement of optimal blood pressure control in non-diabetic patients is more common than in diabetic patients with CKD.

**SPECULATION:** We speculate that the routine laboratory calculation and reporting of estimated GFR will increase the awareness of CKD and increase utilization of treatments, like ACEi/ARBs, in non-diabetics patients with renal disease which will reduce the number of patients developing end-stage renal failure.

**Cervical Cancer Screening among Women with Hysterectomies by Provider Type.** B.G. Lewis, E.A. Halm, and A.D. Federman. Mount Sinai School of Medicine, New York, NY. (Tracking ID # 134166).

**BACKGROUND:** Since 1996, the U.S. Preventative Task Force has recommended against cervical cancer screening in women without a cervix. Yet, as recently as 2002, 69% of such women reported getting a pap smear within the previous 3 years and the factors influencing this pattern of care remain vague. Because both gynecologists and generalists perform pap smears, we examined the association between provider type and pap smear rates among post-hysterectomy women.

**METHODS:** We analyzed data from the 2000 National Health Interview Survey (NHIS), a cross-sectional, nationally representative annual survey of self-reported health and health care utilization among adults (n = 32,374). We included post-hysterectomy women ages 18–65. We excluded those with a history of abnormal pap smears, breast, cervical, endometrial or ovarian cancer, current pregnancy and recipients of Medicare. We determined pap smear rates in the past 12 months, strati-

fied by provider type: generalist (gen); gynecologist (gyn) or both. We used multiple logistic regression to assess the relationship between pap smears and provider type, adjusting for age, race, education, income, insurance status, census region, smoking and health status. SUDAAN statistical software was used to account for the NHIS sampling design.

**RESULTS:** The analysis included 1,221 women, representing 7.3 million women nationwide. 53% received care from a gyn, 26% from gen, and 20% from both. The mean ages of the women were 49 years in gyn, 53 in gen, and 51 in both. Women in the 3 provider groups differed significantly by black race (41%, 33%, 25%;  $p=0.001$ ), married (77%, 67%, 72%;  $p=0.039$ ), uninsured (57%, 32%, 11%;  $p=0.042$ ), urban residence (46%, 29%, 24%;  $p<0.001$ ), and having 1 chronic illness (54%, 26%, 19%;  $p=0.003$ ). They did not differ significantly by income, immigration status, Census region, or smoking status. Overall, 55% had a pap smear in the previous 12 months. 85% of women in the gyn group underwent Pap smears; 44% in gen, and 73% in both gen/gyn ( $p<0.001$ ). In multivariate analysis, women who visited gyn were more likely than those cared for by gen alone to have had a pap smear (Adjusted OR 4.44, 95% CI 2.21–8.91). The effect was less pronounced when women visited both (AOR vs. gen: 1.47, 95% CI 0.62–3.50).

**CONCLUSIONS:** Approximately 4 million pap smears are performed each year on women who have had hysterectomies though cervixes are only left in <5% of cases. Gynecologists perform the majority of these pap smears; however, a large number of such women receiving care from generalists continue to undergo this service. Additional research is needed to identify the physician and patient factors that influence the use of pap smears in post-hysterectomy patients and to prevent unnecessary care.

#### **Comprehensiveness of Preventative Care among Women Seen by Generalists, Gynecologists or Both** B.G. Lewis, E.A. Halm, and A.D. Federman. Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Both gynecologists and generalists provide preventative care to women. However, the effect of provider type on the delivery of preventative care remains unclear. We examined use of preventative services as recommended by the US Preventative Task Force, among women seen by generalists only (gen), gynecologists only (gyn) or both.

**METHODS:** Using cross-sectional data from the 2000 National Health Interview Survey (NHIS), we studied self-reported receipt of preventative services for women ages 18–65 ( $n=10,347$ ). We excluded women with a history of breast, colorectal, cervical, endometrial or ovarian cancer, current pregnancy and recipients of Medicare. For women ages 18–65, we analyzed the association of provider type with rates of pap smears (excluding those with a history of hysterectomy), tobacco use screening and exercise/diet counseling; for women 50–65, biannual clinical breast exams (CBE), mammograms, and colon cancer screening were also analyzed. We modeled each outcome using multivariate logistic regression, and total number of services using Poisson regression, and controlled for age, education, income, race, insurance type, comorbidities. The analysis was weighted to account for the multilevel sampling design of the NHIS.

**RESULTS:** Women seen by gen (15%), gyn (62%) and both (23%) differed by age (43 yrs, 37, 39, respectively,  $p<0.01$ ), black race (18%, 48%, 33%,  $p<0.01$ ), college-education (12%, 61%, 26%,  $p<0.01$ ), and having  $\geq 1$  chronic disease (16%, 60%, 22%,  $p<0.01$ ). The mean number of services by provider type were, for women <50, 1.9 (gyn), 1.5 (gen) and 1.9 (both) ( $p<0.01$ ), and for women 50–65, 4.3 for gyn, 4.0 for gen, 4.2 for both ( $p<0.01$ ). These findings remained significant in adjusted Poisson regressions for women <50 ( $\beta$ : gyn, 0.22,  $p<0.01$ ; both, 0.24,  $p<0.01$ ) and 50–65 ( $\beta$ : gyn, 0.09,  $p<0.01$ ; both, 0.11,  $p<0.01$ ). Women 18–65 seen by gyn or both were more likely to have pap smears (gyn vs. gen, adjusted OR 11.06, 95% CI 6.87–17.80; both vs. gen: 11.47, 6.25–21.07) and tobacco use screening (gyn vs. gen: 1.15, 0.93–1.42; both vs. gen: 1.28, 1.00–1.64). Gyn patients tended to receive diet/exercise counseling less than gen (diet: 0.88, 0.69–1.12; exercise: 0.91, 0.73–1.14). Among women 50–65, gyn and both gyn/gen patients were more likely than gen patients to have mammograms (gyn vs. gen: 2.95, 1.48–5.87; both vs. gen: 3.59, 1.48–8.70) and CBE (gyn vs. gen: 3.31, 1.81–6.04; both vs. gen: 4.38, 2.13–9.03). There was no significant difference in colon cancer screening. Among women 18–65 with no chronic health problems ( $n=1528$ ), receipt of preventative care did not differ significantly except gyn and both continued to perform significantly more mammograms (AOR, 95% CI: gyn: 3.59, 1.52–8.48; both 5.06, 1.72–14.89) and pap smears (gyn: 10.57, 6.00–18.62; both: 10.77, 5.46–21.24) than gen.

**CONCLUSIONS:** Women seen by gyn alone or both gyn and generalists receive more preventative services compared to those seen by generalists alone. Collaborative gyn/generalist care may not be necessary to ensure comprehensive preventative care for many women. Moreover, these findings further validate the role of gynecologists as primary care providers for many women.

#### **Statins, Angiotensin Receptor Blockers, and Steroid Weaning Are Associated with Reduced Mortality among Heart Transplant Recipients.** S.A. Lubitz, D.A. Baran, M.J. Zucker, L.H. Arroyo, M. Chan, M.C. Courtney, R. Correa, D. Spielvogel, S.L. Lansman, and A.L. Gass. Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Immunosuppressive strategies and post-transplant pharmacologic regimens continue to evolve for cardiac transplantation. The current study examined the associations of common post-transplant immunosuppressive and adjunctive medications with the long-term survival of cardiac transplant recipients.

**METHODS:** We reviewed demographic, clinical, and pharmacologic data from 220 consecutive patients that received heart transplants between 1986 and 2003 and survived beyond 3 months. Immunosuppressive regimens were cyclosporine ( $n=94$ ) or tacrolimus ( $n=126$ ) based, and 104 patients were successfully weaned off steroids (all receiving tacrolimus). Significant univariate predictors of mortality ( $p<0.20$ ) were subsequently analyzed in a Cox proportional hazards analysis.

**RESULTS:** The mean follow-up was  $52 \pm 13$  years. Overall survival was 96%, 88%, and 81% at 1, 3 and 5 years, respectively. Significant multivariate associated with mortality included pretransplant diabetes mellitus (hazard ratio [HR] 2.83, 95% confidence interval [CI] 1.45–5.04), black race (HR 1.41, 95% CI 1.01–1.94), higher pre-transplant creatinine clearance (HR 0.99, 95% CI 0.98–1.00), removal from steroids (HR 0.60, 95% CI 0.39–0.85), and exposure to a statin (HR 0.53, 95% CI 0.40–0.70) or ARB (HR 0.50, 95% CI 0.20–0.95) during the post-transplant period. Steroids were weaned an average of 427 days (range 94–3519) after transplantation. The average number of episodes of high-grade rejection (ISHLT 3A/3B) within the first year was similar for patients maintained on steroids and for those weaned off steroids.

**CONCLUSIONS:** Treatment with a statin, an ARB, and steroid weaning were each associated with large mortality benefits. The mortality reductions demonstrated here warrant prospective study.

#### **Ursodeoxycholic Acid for Chemoprevention in Ulcerative Colitis and Primary Sclerosing Cholangitis: A Retrospective Cohort Study.** T. Ullman, L. Maratchi, V. Croog, D. Jaffe, and S. Itzkowitz. Dr. Henry D. Janowitz Division of Gastroenterology, Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Ulcerative colitis (UC) patients carry an increased risk of colorectal cancer (CRC). Patients with primary sclerosing cholangitis (PSC) and UC are at even greater risk. Animal models and two human reports have suggested that ursodeoxycholic acid (UDCA), a synthetic bile acid, may attenuate this risk.

**AIM:** To determine the effect of UDCA use on the development of colonic neoplasia (dysplasia or CRC) in patients with UC and PSC.

**METHODS:** Following IRB approval, patients with both UC and PSC were identified by query of hospital medical records, outpatient records and the Mount Sinai GI pathology database. Medical, endoscopic, and surgical records of all such patients were then reviewed and abstracted for UC history, PSC history, UDCA dose and duration, colonoscopic surveillance history and outcomes. Life tables were constructed with diagnosis of PSC serving as t0 (time at which patients became available to take UDCA) and colonoscopy with flat low-grade dysplasia (LGD), high-grade dysplasia (HGD), or CRC serving as the primary outcome measure. Results were analyzed comparing UDCA users to non-users.

**RESULTS:** We identified 50 patients with UC and PSC, 34 men and 16 women. Among them 32 were UDCA users (UDCA) and 18 were non-users (No UDCA). Mean duration of follow-up was 59.6 months, during which patients underwent an average of 2.1 colonoscopies (UDCA 2.1, No UDCA 2.0). During follow-up, 6 patients developed LGD (5 UDCA users, 1 No UDCA), 2 developed HGD (0 UDCA, 2 No UDCA), and 4 developed CRC (2 UDCA, 2 No UDCA). Actuarially, there was no difference in dysplasia development between the 2 groups; in univariate modeling UDCA users progressed at 0.70 the rate of non-users (95% CI, 0.23–2.17,  $p=0.54$ ). After adjustment for duration and extent, the odds ratio decreased to 0.64, but was still not significant.

**CONCLUSION:** In our population of patients with UC and PSC, UDCA use offered little if any protection against the development of dysplasia. Careful surveillance or prophylactic colectomy is warranted in these patients.

**Attempting to Reduce Inappropriate Vancomycin Use with a Computerized Reminder System.** B. Metzger, A. Derevnuk, U. Conte, and D. Calfee. The Mount Sinai Medical Center, New York, NY.

**BACKGROUND:** Vancomycin-resistant enterococci (VRE) are now responsible for over 25% of all enterococcal nosocomial infections in ICU patients and three cases of vancomycin-resistant *S. aureus*, each carrying the vanA gene from VRE, have been identified in the U.S. Antibiotic overuse is an important risk factor for the development of antimicrobial resistance. National recommendations for the use of vancomycin have been published by CDC-HICPAC but inappropriate use of this antibiotic continues.

**OBJECTIVE:** To determine whether a computerized order entry system-based reminder that utilizes the CDC recommendations could reduce inappropriate use of intravenous vancomycin.

**METHODS:** The Mount Sinai Hospital is a 1,000-bed urban teaching hospital. Baseline data on vancomycin use and its appropriateness were collected over a six-week period (Period 1) on three pilot inpatient wards. The same information was collected during a second six-week period (Period 2) following introduction of a computer-based reminder. During both periods, the medical record of patients receiving vancomycin for >96 hours was reviewed to determine the appropriateness of vancomycin therapy. During Period 2, if patients on the pilot wards received vancomycin for more than 72 hours, a summary of CDC recommendations for appropriate vancomycin use was displayed on the computerized order entry system. On this screen, the clinician was required to indicate if vancomycin would be discontinued or, if not discontinued, to select the appropriate indication for ongoing vancomycin administration. This screen persisted until a selection was made.

**RESULTS:** During Period 1, 31 (38%) of 81 courses of vancomycin were continued longer than 96 hours. Of those, 14 (45%) were inappropriate. Among those 14, the mean duration of therapy was 7.0 days (median = 6.2 days). During Period 2, 36 (44%) of 81 courses of vancomycin were continued longer than 96 hours. Of those 36, 20 (56%) were inappropriate ( $p=0.40$  vs. Period 1). Of those 20, the mean duration was 8.5 days (median = 6.25 days,  $p=0.33$  vs. Period 1).

**CONCLUSIONS:** An intervention that used an existing computerized order entry system to remind clinicians of the CDC recommendations for appropriate vancomycin use was unsuccessful at reducing inappropriate vancomycin use and duration of therapy. Potential limitations of this type of intervention include a lack of a specific educational component and the absence of personal interactions between clinicians and antimicrobial stewardship program personnel.

**Gram Negative Infections.** G. Patel. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

Gram negative infections are common causes of both morbidity and mortality in the hospital. An increasing percentage of these bacteria, especially *Escherichia coli* and *Klebsiella pneumoniae*, have developed extended-spectrum beta-lactamases (ESBL) that render them resistant to penicillins, cephalosporins, and aztreonam—the first line agents used to treat both nosocomial and community acquired infections. The goal of this study was to determine which patients are at risk for these infections and what clinical factors can be modified to reduce the prevalence of these resistant organisms at Mount Sinai Hospital. This is a retrospective analysis comparing the clinical parameters associated with gram negative infections and those associated with infections with gram negative ESBL producing bacteria. From May of 2001 to December of 2004 there were 109 documented cases of bacteremia caused by ESBL producing gram negative rods. Preliminary analysis indicates that prior antibiotic is a risk factor for these infections and there is some suggestion that liver disease, nursing home residence, and central venous catheters may also be risk factors.

**Clinical Experience with Infliximab in the Treatment of Crohn's Disease at Mount Sinai.** J. Potach. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Infliximab (Remicade) is a chimeric monoclonal antibody against TNF-alpha given as intravenous infusion that has been shown to be effective in the treatment of Crohn's disease refractory to standard therapy. However the drug has been associated with many adverse effects, most notably acute and delayed infusion reactions occurring in as many as 15% of recipients. While there have been several randomized trials looking at the safety and efficacy of Infliximab, there is a paucity of data on the performance of the drug in non selected populations that are commonly encountered in clinical practice.

**METHODS:** All patients over the age of 18 who received at least one dose of Infliximab for the treatment of Crohn's disease at The Mount Sinai Medical Center between October 1, 1998 and October 1, 2004 were eligible to participate. A comprehensive review of the patients' chart at the clinical infusion center was performed. Data were gathered on the number and schedule of infusions, dose, presence or absence of infusion reactions, treatment and prophylaxis of infusion reactions and ability to continue to receive Infliximab despite reactions. Following the chart review, patients were mailed two questionnaires. The questionnaires assessed for both response to therapy and the presence of adverse health events in the time period following infusion.

**RESULTS:** A total of 318 patients received 1596 infusions during the study period. 98 patients (30.6%) had an infusion reaction. 79.5% of reactions were classified as acute or occurring within 24 hours of the infusion. The major symptoms were flushing, chest tightness and dyspnea. Only 0.5% of the infusions complicated by a reaction were unable to be completed after giving medications to alleviate the symptoms. There were no infusion related hospitalizations or deaths. However 40% of patients who had an infusion reaction did not receive additional therapy with Infliximab. The concurrent use of immunomodulating agents such as systemic corticosteroids and 6-mercaptopurine led to a non-significant trend in the reduction of infusion reactions. There was a non-significant decrease in the rate of infusion reactions in patients who were on fixed interval dosing schedules. Collection of data regarding efficacy of Infliximab and long-term adverse health effects is ongoing.

**CONCLUSIONS:** The use of Infliximab for Crohn's disease is safe. Although infusion reactions are common, they can almost always be treated and do not prevent the completion of the infusion. However infusion reactions may lead to decreased patient willingness to receive subsequent doses of the drug. The use of immunomodulating agents and fixed interval scheduling of doses leads to a non-significant reduction in infusion reactions.

**Effects of HIV on Bone Mass in the Elderly.** D. Restrepo<sup>1</sup>, S. Jones<sup>1</sup>, A. Kasowitz<sup>1</sup>, D. Korenstein<sup>1</sup>, S. Wallenstein<sup>2</sup>, A. Schneider<sup>1</sup>, and M. Keller<sup>1</sup>. Departments of <sup>1</sup>Medicine and <sup>2</sup>Biostatistics. Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Patients infected with HIV have experienced a dramatic decrease in morbidity and increase in life expectancy since the introduction of highly active anti-retroviral therapy (HAART). The advent of HAART coupled with effective prophylaxis for opportunistic infections has resulted in a dramatic increase in survival. As the HIV-infected population gets older, chronic illnesses are becoming an important part of HIV care. In parallel, there has been a progressive increase in the mean age of patients infected with HIV. 1–2% of newly diagnosed HIV disease occurs in individuals > 65 years of age and 10–15% involve patients > 50 years old. It is particularly important, in view of their near-normal lifespan, to examine the skeletons of elderly HIV patients who are already at high-risk for involutional osteoporosis.

The potential impact of chronic HIV infection on fracture risk began to receive attention after the report of two cases of low impact fractures and a case of osteonecrosis in young men with HIV who had been treated with HAART. Initial clinical and laboratory evidence suggests that HIV-infected patients with or without treatment may be at increased risk for osteoporosis. Antiretroviral side effects, prolonged exposure to HIV and/or activated immune cells are all possible causes for this observed association. The specific aim of this study is to compare a cohort of elderly HIV-positive females and males with matched HIV-negative controls to determine differences in bone mineral density and biochemical markers of bone turnover.

**METHODS:** 64 HIV-infected and 64 HIV-negative subjects matched by age (within 2 years), sex and race are being recruited from the Infectious Disease and Internal Medicine clinics at the Mount Sinai School of

Medicine. Participants undergo a detailed medical and medication history, physical examination (including assessment of the body mass index and waist circumference) and dietary calcium intake survey at the General Clinical Research Center. Subjects with illnesses or medication use known to affect bone mass are excluded. Laboratory evaluation is performed in order to assess gonadal status, vitamin D levels, parathyroid function and bone turnover. Bone mineral density at the LS spine and femoral neck, instant vertebral assessment (IVA), and markers of bone turnover are being compared between the HIV-positive subjects and HIV-negative controls using the student's *t* test. Multivariate analysis will be used to control for known and potential confounders of bone mass.

**RESULTS:** A total of 80 subjects have completed the study (48 HIV-positive cases and 32 HIV-negative controls. Of 17 matched pairs, the mean age is 60 years, 13 are female, and 4 are male. There are 9 Hispanics, 5 Blacks and 3 Whites. Among the HIV-infected subjects, 9 are on protease inhibitors and 8 are not. For the T and Z scores of the hip and spine, the cases have lower values than the controls and the differences are statistically significant.

**CONCLUSIONS:** Elderly women and men infected with HIV may have lower bone mass than age, race, and sex matched HIV-negative controls. Multiple regression analysis will be used to determine the relationship between bone mineral density and the viral load, CD4 count, duration of HIV infection, abdominal circumference and use and duration of specific classes of antiretroviral agents.

**Intracoronary Stenting Prior to Non-cardiac Surgery.** B.A. Sealove, R. Vilca, S.K. Sharma, M.C. Kim, and W.L. Duvall. Mount Sinai Medical Center, New York, NY.

**BACKGROUND:** While percutaneous coronary intervention (PCI) is a commonly utilized risk-reduction strategy prior to non-cardiac surgery, concern has been raised regarding the safety of surgery in the six weeks following intracoronary stents due to stent thrombosis. The data predates the modern era of antithrombotic therapy used during PCI, and the outcomes of patients treated with GP IIb/IIIa inhibitors, clopidogrel, and heparin-coated stents are unknown.

**OBJECTIVE:** To determine the clinical outcomes of patients at our institution who underwent non-cardiac surgery following PCI in the modern era of stent and antithrombotic therapy.

**METHODS:** A total of 104 patients who underwent 108 non-cardiac surgeries were identified through the use of hospital billing records and the cardiac catheterization laboratory database at our institution. Over a three-year period (2000–2003), each patient had a pci within six months prior to a non-cardiac surgical procedure. Medical records were used to determine patients' antiplatelet and antithrombotic therapy as well as adverse cardiovascular outcomes seven and 30 days following surgery.

**RESULTS:** Overall, 14 patients (13%) suffered an adverse event, with only one episode of stent thrombosis (0.92%). At 30 days post surgery, four patients had died (3.7%), one from cardiac causes (0.92%), six suffered a mi (5.6%), eight suffered cardiac ischemia (7.4%), three had repeat revascularization procedures (2.7%), and six had CHF (5.6%). Surgery occurred three to 180 days following PCI (median 45 days), with 47% of surgeries occurring within six weeks of PCI. There was no discernable pattern to the frequency of adverse events based on the duration of time from PCI to surgery (50% of the adverse events occurred within six weeks of PCI and 50% after six weeks).

**CONCLUSIONS:** The current study, performed during a more modern antithrombotic era, demonstrated no trend of increased adverse cardiac events in patients who underwent non-cardiac surgery soon after PCI. The rate of stent thrombosis was lower than in previously published reports (1.9% and 17.5%) and the overall mortality was comparable or lower (4.0% and 20%). This data suggests that with careful attention to antiplatelet therapy and more current stenting techniques, it may be safe to undergo non-cardiac surgery within six weeks of PCI. Further investigation using drug-eluting stents prior to non-cardiac surgery are underway.

**How Well Do Health-Care Providers Recognize and Treat Sepsis in Hospitalized Patients?** A.K. Sutherland, D. Nierman, and D.A. Kaufman. Mount Sinai School of Medicine, New York, NY.

**INTRODUCTION:** Sepsis is defined as a documented or suspected infection associated with signs of systemic inflammation. Severe sepsis is sepsis with evidence of organ dysfunction, and septic shock is sepsis with acute circulatory failure unexplained by other causes. These syn-

dromes are prevalent among hospitalized patients, and cause a heavy burden upon society both in terms of loss of life and health care expenditures. A usual prodrome of sepsis is systemic inflammatory response syndrome (SIRS), which is characterized by abnormalities of at least two of the following values: temperature, heart rate, respiratory rate, or white blood cell count. In one study, 68% of patients admitted to 3 medical wards during a 9-month study period had SIRS. Of these patients, the prevalence of sepsis, severe sepsis and septic shock was 26%, 18% and 4%, respectively. The overall hospital mortality rate for patients with severe sepsis in 1995 was 28.6%, which accounted for 9.3% of all deaths in the U.S. that year. In an effort to improve outcomes for patients with sepsis, several international critical care medicine organizations formulated the Surviving Sepsis Campaign, publishing evidence-based guidelines for the diagnosis and care of patients with all stages of sepsis. These guidelines recommend the early identification and treatment of sepsis. In particular, based on the findings of a randomized controlled trial, the guidelines advocate early goal-directed therapy (EGDT), which is aimed at rapidly achieving normal circulation and perfusion.

Data from the Mount Sinai Hospital demonstrate that patients admitted to the medical ICU (MICU) from the hospital ward have a higher mortality rate than patients admitted from the Emergency Department. These data are consistent with findings from other investigators. Our anecdotal experience suggests that the diagnosis and treatment of sepsis is often delayed among patients on the hospital wards. Previous studies have associated delays in treatment with worse outcomes for critically ill patients. Other studies have associated delayed treatment of sepsis with worse outcomes.

As a quality assurance initiative, we sought to evaluate whether there are delays in the recognition and initiation of treatment of sepsis, severe sepsis and septic shock among hospitalized patients who required transfer from the general ward to the MICU. We looked at whether the treatments administered on the general hospital wards were consistent with the Surviving Sepsis Campaign guidelines. We chose to focus on sepsis, severe sepsis and septic shock both because of their prevalence and high rates of associated morbidity and mortality, and because there are now clear guidelines that can assist in measuring the timeliness and quality of care provided.

**METHODS:** Two investigators screened all consecutive admissions to the MICU for patients who met 1991 Consensus Conference definitions for severe sepsis or septic shock at the time of MICU admission. We retrospectively reviewed the paper and electronic medical records of each patient with either severe sepsis or septic shock at the time of ICU admission. We noted all recorded vital signs, clinical events, clinicians' impressions and responses, and all laboratory abnormalities. We then reviewed each record to determine when clinicians diagnosed sepsis, severe sepsis or septic shock, what interventions they ordered and when consultation from the Critical Care Medicine service was requested. We then determined the timing of these diagnoses and interventions relative to the first clinical manifestation of sepsis, severe sepsis or septic shock and ICU admission. We also noted whether the treatments administered followed the evidence-based guidelines published by the Surviving Sepsis Campaign.

**SPECIFIC AIMS:** This study was designed to observe caregivers' recognition of sepsis, severe sepsis or septic shock and their responses to the abnormal findings associated with these syndromes. Our observations are important in determining how best to focus the educational and patient care efforts of the Mount Sinai Hospital's MARS team. In addition, we plan to submit the findings of our study for presentation in abstract form at a national meeting and then submit our data for publication. By publicly sharing our data and observations, we hope to contribute to the international effort to improve outcomes for patients with sepsis by drawing attention to the quality of care provided for these critically ill patients.

**Cardiovascular Disease and Modification of Traditional Cardiovascular Risk Factors in Early Chronic Kidney Disease: Data from the National Health and Nutrition Examination Survey, 1999-2000.** C.M. Wyatt<sup>1</sup>, Q. Xu<sup>2</sup>, and R.R. Arons<sup>2</sup>. <sup>1</sup>Division of Nephrology, Mount Sinai School of Medicine, New York, NY, and <sup>2</sup>Mailman School of Public Health, Columbia University Medical Center, New York NY.

**CONTEXT:** Chronic kidney disease affects 10% of US adults, and individuals with early stages of chronic kidney disease are more likely to die of cardiovascular disease than to progress to end-stage renal disease.

**OBJECTIVE:** This study investigates the prevalence of cardiovascular disease and cardiovascular risk factors, and the adequacy of risk factor modification among U.S. adults with early chronic kidney disease.

**DESIGN, SETTING, AND PATIENTS:** The National Health and Nutrition Examination Survey (1999–2000) provides nationally representative data on the health status of the non-institutionalized civilian US population.

**MAIN OUTCOME MEASURES:** The prevalence of cardiovascular disease and cardiovascular risk factors was compared between stages of chronic kidney disease as defined by the National Kidney Foundation. The adequacy of risk factor modification was described among individuals with early chronic kidney disease (Stage 1–3).

**RESULTS:** The prevalence of cardiovascular disease and traditional cardiovascular risk factors increases with increasing stage of chronic kidney disease. After adjusting for demographics and traditional cardiovascular risk factors, early chronic kidney disease remains associated with an increased risk of cardiovascular disease (OR 1.71, 95% CI 1.24–2.37), as well as an increased prevalence of hypertension (OR 1.90, 95% CI 1.42–2.55) and diabetes (OR 2.87, 95% CI 2.06–3.99). The association between early chronic kidney disease and cardiovascular disease, hypertension, and diabetes was not affected by the addition of hypoalbuminemia and elevated C-reactive protein to the model. Only 13% of US adults with early chronic kidney disease achieve combined goals for the management of hypertension, hypercholesterolemia, and diabetes.

**CONCLUSIONS:** Early chronic kidney disease is associated with a high prevalence of cardiovascular disease, even after adjusting for the increased prevalence of cardiovascular risk factors. Further studies are needed to elucidate novel risk factors and to determine the effect of improved cardiovascular risk modification on mortality and morbidity in this high-risk population.

## Case Reports

**End-Stage Liver Disease Is a Chronic Illness.** T. Bishop. Mount Sinai School of Medicine, New York, NY.

End-stage liver disease is a chronic illness that is fatal if not treated with liver transplantation. Many patients experience chronic symptoms during the course of their disease. These symptoms include ascites, pain, confusion, dyspnea, peripheral edema. Other abnormalities that require long term management include hyponatremia, coagulopathies, and renal dysfunction. This article will review the current recommendations for managing long term symptoms in the cirrhotic patient.

**Disseminated Histoplasmosis in Five Immunosuppressed Patients: Clinical, Diagnostic, and Therapeutic Perspectives.** D. Caplivski, C. Salama, S. Huprikar, and E.J. Bottone. Division of Infectious Diseases, Mount Sinai Medical Center, New York, NY, and Elmhurst Hospital Center, New York, NY.

**OBJECTIVES:** Disseminated histoplasmosis is a relatively uncommon manifestation of a disease that primarily affects immunocompromised hosts. We reviewed five cases of disseminated histoplasmosis and examined the strategies that were used to establish a diagnosis in each case.

**METHODS:** Five immunosuppressed patients (four with AIDS and one with a liver transplant) presented with fever, pancytopenia, elevated lactate dehydrogenase (LDH), and nodular pulmonary infiltrates (one miliary pattern). One patient had concomitant diffuse papular and purpuric skin lesions. All five originated from areas of Histoplasma endemicity (Puerto Rico, El Salvador, Brazil, and the Dominican Republic).

**RESULTS:** While histoplasmosis was suspected clinically and epidemiologically, diagnosis was primarily achieved by visualization of phagocytosed Histoplasma yeast cells in peripheral blood smears, bronchoalveolar lavage, and in biopsy specimens. All four AIDS patients showed elevated urine Histoplasma antigen and LDH levels, whereas the liver transplant recipient had a false negative urine Histoplasma antigen and a normal LDH. With the exception of one AIDS patient (in whom diagnosis was delayed), all responded to induction therapy with amphotericin B followed by itraconazole.

**CONCLUSIONS AND SUMMARY:** Disseminated histoplasmosis should be suspected in immunosuppressed individuals who originate from areas of endemicity and present with pancytopenia, fevers, nodular infiltrates, and elevated LDH.

**Prolonged Anticholinergic Toxicity after benztropine (Cogentin) Overdose: Case Report** L.H. Pai. Department of Medicine, Mount Sinai School of Medicine, New York, NY.

**BACKGROUND:** Benztropine mesylate (Cogentin) is an anticholinergic drug commonly used to lessen extrapyramidal symptoms in patients taking major tranquilizers and in those with Parkinson's disease. The abuse and overdose of benztropine is well reported in medical literature. However, physicians remain poorly aware of anti-cholinergic abuse. A case report of a 23-year-old woman who ingested benztropine in a suicide attempt is presented. Delirium and anti-cholinergic manifestations persisted for four days requiring prolonged hospitalization.

**CASE:** A 23-year-old female with a history of depression was brought into the emergency room by her husband after being found confused, agitated, and hallucinating at home. A vial of her mother-in-law's benztropine tablets was found uncapped and empty at bedside. It was presumed that the patient had ingested her mother-in-law's benztropine in a suicide attempt. On admission patient was found confused, agitated, and mumbling incoherently. She had visual hallucinations and was persistently plucking at imaginary objects. She was not following or responding to any verbal commands. Vital signs, labs, ekg and head CT were unremarkable. On physical examination, pupils were dilated (5mm and sluggish) and mucous membranes were dry. A decision was made to not give activated charcoal secondary to aspiration risks and to monitor her on telemetry with a 1:1 observation. The first two days of hospitalization were characterized by agitation, active hallucinations, and combativeness. She also exhibited signs of psychomotor agitation, picking at her sheets. On the third day, she was more alert and oriented but continued to have disorganized thought process and was still delirious intermittently. On the fourth day, patient appeared more lucid. Patient recalled arriving at the hospital and acknowledged that she acted impulsively and regretted her actions. She was transferred to Psychiatry and discharged to home four days later.

**CONCLUSION:** Benztropine has been extensively used in this country, however, therapeutic serum benztropine concentrations are not defined. There have been no studies characterizing its pharmacokinetics. However, a long duration of effect is noted when using this agent. Benztropine overdose has been reported to persist for several days and is in keeping with the long duration of action that has been noted at therapeutic doses. Our experience in taking care of this patient also validate reported literature of long duration of effect of anticholinergic toxicity from benztropine overdose.

**O1 and Non-O1 *Vibrio cholerae* Bacteremia Produced by Hemolytic Strains.** D. Restrepo, S.S. Huprikar, K. VanHorn, and E.J. Bottone. Division of Infectious Diseases, Departments of <sup>1</sup>Medicine, <sup>2</sup>Pathology, and <sup>3</sup>Microbiology, The Mount Sinai Hospital, New York, NY.

Strains of *Vibrio cholerae* that agglutinate with antiserum O1 or O139 (O1 and O139) are the etiologic agents of cholera, a toxin-mediated acute diarrheal illness. Strains of *V. cholerae* that do not agglutinate in O1 or O139 antisera (non-O1) typically cause diarrheal illness mediated by toxins distinct from the cholera toxin. Although non-O1 *V. cholerae* bacteremia is fairly well described, *V. cholerae* O1 bacteremia is rare since this serogroup is not regarded as an invasive organism. In the summer of 2003 we observed two cases of *V. cholerae* (an O1 and a non-O1) bacteremia following diarrheal illnesses in immunocompromised patients with liver cirrhosis residing in New York City. In this report we describe their clinical presentation and conjecture that the hemolytic properties of the *Vibrio* isolates contributed to their ability to invade the bloodstream.

## Health Services Research

**Revascularization Decisions after Coronary Angiography at Mount Sinai Medical Center: A Survey.** I. Nash<sup>1</sup> and C. Rahilly<sup>2</sup>, <sup>1</sup>Cardiovascular Institute and <sup>2</sup>Department of Medicine, Mount Sinai School of Medicine, New York, NY.

**OBJECTIVE:** To elicit referring physicians' perceptions of their involvement in coronary revascularization decisions in patients whom they have referred for coronary angiography.

**BACKGROUND:** Internists or non-interventional cardiologists referring their patients for coronary angiography have variable input into subsequent revascularization decisions. To our knowledge, no researcher at Mount Sinai or elsewhere has sought to elicit how involved referring doctors perceive themselves to be in coronary revascularization decisions in their patients.

**METHODS:** We have developed a survey designed to procure referring physician's expectations regarding their involvement in revascularization decisions for their patients undergoing coronary angiography. Each member of Mount Sinai's Department of Medicine will receive a survey and an accompanying letter, asking for their voluntary participation in the survey. The survey consists of some initial questions requesting information regarding specialty training and volume of patients referred to Mount Sinai's cardiac catheterization laboratory for coronary angiography. Remaining questions seek to elicit referring doctors' perceptions of their involvement in revascularization decisions in their patients whom they have referred for coronary angiography, and what process by which such physicians would prefer such decisions are made. The survey is anonymous, and responses will not be identifiable to participants.

**ANALYSIS:** The results of the survey will be summated and presented in a qualitative fashion. Analysis will determine the frequency by which one process versus another is used to make revascularization decisions (such as the interventional cardiologist making revascularization decisions at the time of the angiogram, versus discussing the findings of the angiogram with a referring internist first), according to perceptions of referring physicians. Analysis will also determine whether the process by which revascularization decisions are made reflect what referring physicians consider the "best" process for making such decisions.

## Public Health / Epidemiology Research

**Senior Citizen Travel: An Analysis of the Geosentinel (GeoS) Surveillance Network.** K.D. Sigel<sup>1</sup>, G. Rosselot<sup>1</sup>, L. Weld<sup>2</sup>, P. Pandey<sup>3</sup>, M. Schunk<sup>4</sup>, B. Connor<sup>5</sup>, M. Shaw<sup>6</sup> and A. Gurtman<sup>1</sup>, for the Geosentinel Surveillance Group. <sup>1</sup>Department of Medicine, Mount Sinai School of Medicine, New York, NY, <sup>2</sup>Division of Global Migration and Quarantine, Centers for Disease Control and Prevention, Atlanta, GA, <sup>3</sup>CIWEC Clinic Travel Medicine Center, Kathmandu, Nepal, <sup>4</sup>University of Munich, Munich, Germany, <sup>5</sup>Weill Medical College of Cornell University, New York, NY, and <sup>6</sup>Worldwide Travellers Health and Vaccination Centre, New Zealand.

**OBJECTIVES:** There is a dearth of literature examining travel related illness in the elderly population. The purpose of this study is to determine demographic and clinical characteristics of elderly travelers, by utilizing data collected at Geosentinel surveillance network clinics.

**METHODS:** The population studied was all Geosentinel travelers aged 65 and older (excluding those with only immigration as a reason for travel). The comparison group was all Geosentinel travelers aged 25–44. Univariate and multivariate analyses were performed to determine differences in demographics, diagnoses, and clinical presentation amongst the comparison groups. Statistical significance was determined with chi-squared and logistic regression analyses.

**RESULTS:** A total of 1,201 travelers aged 65 and older were included in the analysis, as well as 16,542 travelers aged 25 through 44, as a comparison group. The elderly travelers in the GeoS database were primarily traveling for tourism, and were significantly less likely to have had a pretravel encounter than their younger counterparts. (50% vs. 65%,  $p < 0.001$ ) The most common diagnoses were similar amongst the two groups, with respiratory infections and acute diarrhea being very common. The older travelers presented significantly less acute diarrhea than the younger travelers (22% vs. 14%,  $p < 0.01$ ) and more respiratory illnesses (10% vs. 14%,  $p < 0.01$ ), and their respiratory illnesses appear to have been more severe. The elderly travelers were significantly more likely to present after travel with a dermatologic, cardiac, or respiratory chief complaint, and were less likely to present with gastrointestinal, fever-related, ENT-related, genitourinary, or fatigue-related chief complaint. Elderly GeoS travelers with acute diarrhea were significantly more likely to present with a cardiac complaint, (OR 5.1,  $p = 0.02$ ), or a respiratory complaint (OR 2,  $p = 0.03$ ) than younger GeoS travelers with acute diarrheal illness. Elderly travelers with diarrhea were significantly more likely to have traveled to South America (OR 2,  $p = 0.04$ ) and South Central Asia (OR 2.23,  $p(0.01)$ ), than elderly trav-

elers without diarrhea. Elderly travelers with STD's were much more likely to have traveled to SE Asia (OR 3.6,  $p = 0.05$ ) than other travelers aged 65 and older without STD diagnoses, and those with malaria were much more likely to have traveled to sub-Saharan Africa (OR 6.4,  $p = 0.01$ ) than elderly travelers without malaria.

**CONCLUSIONS:** Elderly travelers in the GeoS have many of the same illnesses as their younger counterparts, but present with a different spectrum of complaints, and amongst their different diagnoses exhibit different patterns of travel.

## Translational Research

**Seminal Fluid Proteins Interfere with the Anti-HSV Activity of Candidate Microbicides in Clinical Development.** S. Patel<sup>1\*</sup>, M. Keller<sup>1</sup>, K. Hogarthy<sup>1</sup>, A. Tuyama<sup>2</sup>, M.J. Carlucci<sup>2</sup>, E. Fam<sup>2</sup> and B.C. Herold<sup>2</sup>. Departments of <sup>1</sup>Medicine and <sup>2</sup>Pediatrics, Mount Sinai School of Medicine, New York, NY. (\*SP is a Doris Duke Medical Student Scholar)

**INTRODUCTION:** Currently there are over 40 million people living with HIV/AIDS; heterosexual transmission accounts for the majority of new cases. This epidemic is fueled by a parallel epidemic of genital herpes infection. Epidemiological studies demonstrate that HSV infection increases the risk of HIV acquisition and that co-infection with HIV and HSV increases both HIV transmission and replication. Current options are limited to condom use, which is often difficult for women to negotiate. Therefore, the development of topical microbicides, compounds designed for vaginal application to prevent acquisition and transmission of HIV and HSV, is a major health priority. Microbicides currently in Phase II/III clinical trial include several polyanion compounds that bind to the viral glycoproteins gp120 of HIV and gB of HSV-2 to block binding and entry. These compounds inhibit HIV and HSV in cell culture, organ explants and animal models. However, while their activity is preserved in the presence of cervicovaginal secretions and over a broad pH range, no study has assessed the anti-viral activity if virus is introduced in seminal fluid. Seminal fluid is alkaline and contains ~25 mg/mL protein, many of which are unique to semen. The purpose of this study is to test the anti-HSV activity of candidate microbicides if virus is introduced in the presence of seminal fluid using cell culture assays and a murine model.

**METHODS:** Clinical specimens were obtained from healthy individuals, ages 18–50, after obtaining informed consent. HSV plaques assays were performed on human cervical epithelial (CaSki) cells. Microbicides evaluated included PRO 2000, a sulfonated naphthalene compound currently in two large-scale Phase II/III trials, SAMMA, a non-sulfonated anionic mandelic acid, and SpM8CHAS, a sulfonated amphiphilic umbrella compound. Cells were pre-treated for 1 hour at 37°C with one of the three compounds diluted in PBS or cervicovaginal lavage fluid (CVL). HSV-2 isolates were then introduced in PBS, seminal plasma, or a control HEPES buffer adjusted to the pH and protein concentration of seminal plasma. The cells were again incubated for 1 h at 37°C. Infection was monitored by counting plaques at 48 h. For murine studies, mice were pretreated with a single dose of medroxyprogesterone 5 days prior to application of formulated PRO2000 and then challenged 15 min later with virus diluted in PBS or seminal fluid. Mice were monitored for signs and symptoms of genital herpes and sacrificed if significant genital ulcers or neurological disease developed.

**RESULTS:** There was a significant and substantial loss of anti-HSV activity for PRO 2000 (unformulated and formulated drug) and SAMMA if virus were introduced diluted in seminal fluid compared to matched control buffer or PBS. The anti-viral activity of Spm8CHAS was also reduced, but to a lesser extent. The interference observed with seminal fluid persisted in the presence of CVL, which itself has intrinsic anti-HSV activity. A fluorescence assay, which measures free PRO 2000, indicates that seminal proteins, but not albumin, bind PRO 2000. In contrast, blood serum proteins did not interfere with microbicide activity, suggesting that a unique seminal fluid protein(s) mediated the interfering activity. Fractionation studies using Centricon preps indicated that the interfering proteins are higher molecular weight (~100kD). Mass spectrophotometry studies are ongoing to identify proteins in this fraction. Preliminary murine studies suggest that the interference observed *in vitro* translates to a reduction in effectiveness *in vivo*: PRO 2000 2% gel protects 80% (4/5) mice if virus is introduced in PBS but only 40% (2/5) mice if virus is introduced in seminal plasma.

**CONCLUSION:** These studies demonstrate that high molecular weight protein(s) found in seminal fluid bind to anionic microbicides reducing their effectiveness in cell culture and in a murine model. If validated in ongoing human clinical trials, identifying the interfering protein(s) and mechanism of action should facilitate development of formulations to overcome this phenomenon.

## Jersey City Medical Center

**The Effect of Moving to a New Hospital on the Prevalence of Resistant Bacteria.** C. Tadors<sup>1</sup>, R. Guerrero<sup>2</sup>, A. Gregoriu<sup>1</sup>, and C. Strand<sup>2</sup>. Departments of <sup>1</sup>Medicine and <sup>2</sup>Pathology. Jersey City Medical Center, Jersey City, NJ.

**INTRODUCTION:** The influence of hospital design on nosocomial transmission of resistant bacteria has not been formally studied. Our hospital's relocation in May 2004 to a new building, with new and different ward and ICU designs, prompted us to study the antimicrobial susceptibility patterns in the new vs. the old hospital.

**METHOD:** The method used is a laboratory information system search of patient results with determination of cumulative susceptibility of pathogens recovered from inpatients and outpatients in the new vs. the old hospital. The study examines these patients' antibiograms over a 12-month period, before the move, and in the 9-month period after the relocation. Only data for organisms with more than 10 isolates is included. The study follows the CLSI guidelines for antibiograms using only first isolates per patient per stay.

**RESULTS:** The gram-positive organisms was found to have no significance in susceptibility pattern in the old vs. new hospital. However, for the gram-negative organisms, *A. baumannii* was more susceptible to Amikacin and Imipenem in the new vs. the old one. The other common gram-negative bacteria showed no significant difference.

**CONCLUSION:** Radical facility design changes, which enhance optimal infection control practices, in our study led to a significant improvement in sensitivity of *A. baumannii*. However, the data show no change in the prevalence of resistance in other gram-negative or gram-positive bacteria.

**Comparison of Antimicrobial Resistance Patterns of Three Hospitals.** M. Fernandez<sup>1</sup>, R. Guerrero<sup>2</sup>, L. Vaccaro<sup>3</sup>, A. Grigoriu<sup>1</sup>; C. Strand<sup>2</sup>, N. Go<sup>1</sup>, R. Munera<sup>2</sup>, S. Nayak<sup>2</sup>, and A. Khan<sup>2</sup>. Departments of <sup>1</sup>Medicine, <sup>2</sup>Pathology and <sup>3</sup>Infection Control. Jersey City Medical Center, Jersey City, NJ.

**INTRODUCTION:** The antimicrobial susceptibility patterns from the three LibertyHealth hospitals were evaluated by analyzing retrospectively each hospital's antibiogram over a two-year period.

**OBJECTIVE:** To compare resistance patterns of three hospitals belonging to one hospital system located in Hudson County, NJ.

**METHOD:** The antimicrobial susceptibility testing followed standard guidelines using the Vitek 2.

**RESULTS:** The results showed narrow range of susceptibility (44–54%) for methicillin resistant *Staphylococcus aureus* in the 3 hospitals. *Enterococcus faecalis* susceptibility rates to ampicillin were similar (97–100%) as well as for vancomycin (88–92%). *Escherichia coli* was the most common gram-negative isolate in all 3 hospitals, followed by *Pseudomonas aeruginosa*. The ampicillin sensitivities of *E. coli* were in Jersey City Medical Center (JCMC) (42%) Meadowlands Hospital (MH) (53%) and Greenville Hospital (GH) (37%) and the Trimethopim/Sulfa susceptibilities were also comparable (65–71%). *P. aeruginosa* susceptibilities to cefepime varies: JCMC (44%), MH (33%) & GH (57%); ceftazidime susceptibilities were JCMC (44%), MH (64%) & GH (57%). *Acinetobacter baumannii* was a common isolate and was highly resistant to ampicillin/sulbactam at JCMC (48%), MH (61%) & GH (58%) as well as to amikacin at JCMC (44%), MH (42%) & GH (44%).

**CONCLUSION:** There are important differences in prevalence and antimicrobial susceptibility patterns of the Gram-positive bacteria and Gram-negative bacteria isolated from the three hospitals. This strongly suggests multiple mechanisms of resistance.

**Knowledge of Medical Residents about Hospice and Palliative Care: A Brief Survey.** S. Hosadurga, H.D. Park, X. Mdluli, J. Shah, T. Borisiak, and M. Reisner. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**BACKGROUND:** Palliative and hospice care has become a more essential element of patient care as the aging population increases. In November 2004, a brief survey was done for the 32 internal medicine residents at Jersey City Medical Center regarding knowledge about palliative and hospice care.

**RESULTS:** 94% of residents have no experience of hospice care outside of the hospital setting. 85% of residents did not clearly understand the composition of core hospice team. 66% of residents showed lack of knowledge about the continuation of hospice benefits after patient is deceased. 60% of residents misunderstood the role of PED tube for the hospice patient.

**CONCLUSION:** This study demonstrated fundamental lack of knowledge about hospice and end-of-life care among the medical residents. As the aging population increases, education for hospice and end-of-life care should be prioritized.

**The Pathogen Microorganisms Frequency and Antibiogram in Jersey City Medical Center New Neonatal Intensive Care Unit (NICU) as Compared to the Old NICU.** J. Padilla<sup>1</sup>, P. Patel<sup>1</sup>, S. Umaru<sup>1</sup>, C. Strand<sup>2</sup>, S. Alsheikh<sup>1</sup>, S. Puvabanditsin<sup>1</sup>, and R. Guerrero<sup>2</sup>. Departments of <sup>1</sup>Medicine and <sup>2</sup>Pathology. Jersey City Medical Center, Jersey City, NJ.

We studied the frequency of specific microorganisms and antimicrobial susceptibility of the first isolates as recommended by the NCCLS for the Jersey City Medical Center old NICU (1/2002–5/16/2005: 28 months) vs. the new NICU (5/2004–2/2005: 8 1/2 months). The study data shows that coagulase negative *Staphylococcus* (CNS) is the leading cause of sepsis in both periods/unit representing 47% (old) and 36% (new) of the total isolates (81 and 66). There is an increase in isolation of *Staphylococcus aureus* in our new NICU, it represents 29% of the isolates compared to 15% in our old NICU. *Pseudomonas aeruginosa* represents 18% (new) and 12% (old) followed by *Escherichia coli* 11% (new) and 13% (old); *Serratia marcescens* 6% (new) and 10% (old).

Important observations based on this data are: (a) Oxacillin sensitive coagulase negative *Staphylococcus* is 14% in our new NICU compared to nil in our old NICU; (b) Oxacillin-sensitive *S. aureus* are 79% (old) and 68% (new) isolates. There is a spike increase in methicillin-resistant *S. aureus* (MRSA) in our NICU; (c) Gentamicin-sensitive *P. aeruginosa* is 92% in the new NICU compared to 78% in our old NICU. (d) Gentamicin/Tobramycin-sensitive *E. coli* is 71% in our new NICU compared to 100% in our old NICU.

**Emergent Chemotherapy as a Modality of Treatment for Symptom Reduction in Massive Hemoptysis from Small Cell Carcinoma Impinging on the Left Atrium and Pulmonary Veins.** R. Dharmaji, P. Venkataswamy, A. Reddy, H.D. Park, and J. Matta. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**LEARNING OBJECTIVES:** Recognize hemoptysis as a presenting sign of small cell carcinoma metastasizing to left atrium and pulmonary veins. Recall that emergent chemotherapy has a role in symptom reduction.

**CASE:** A 41-year-old African-American male with no prior medical history, who smoked one pack per day for more than 15 years, comes with chief complaint of cough with blood streaked sputum for 2–3 days, which transforms into a full-blown hemoptysis within few hours of admission. Initial bronchoscopy showed massive hemoptysis, the exact source of bleeding could not be visualized. Emergent arteriogram for embolotomy to arrest the bleeding site was unsuccessful. CT chest showed a 4x5 cm irregular mass abutting the left atrium and the pulmonary veins. Patient underwent open lung biopsy and the frozen section of the specimen was identified as a small cell carcinoma, which later was confirmed by the pathologist. Emergent chemotherapy with cisplatin given for three days resulted in complete stoppage of hemoptysis with rapid recovery and resulting in extubation.

**DISCUSSION:** Emergent chemotherapy has a role in the tumor shrinkage resulting in reduced risk of hemoptysis. In one review (1997), mesothelioma, melanoma, lung cancer and renal neoplasms were most likely to metastasize to the heart. Among lung cancer, anaplastic small cell and adenocarcinoma showed the most frequent heart involvement in males, while squamous cell carcinoma was more

common in females. Our patient, who had small cell carcinoma, responded well to emergent chemotherapy resulting in tumor shrinkage.

**Markedly Elevated CA-19-9, Does Not Always Indicate Pancreatic Cancer.** S. Soosaimanickam, C. Valle, M. Koehn, P. Thiruvilwamala, R. Chinai, and P. Weissman. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**INTRODUCTION:** The tumor marker CA 19-9 is based on monoclonal antibody to colonic carcinoma cell lines. CA 19-9 is expressed in pancreatic carcinomas. It is also found in normal pancreas and in chronic pancreatitis. Here is a case of pancreatic disease where CA 19-9 was marked elevated and yet proved to be a benign lesion.

**CASE:** A 33-year-old male with no medical history presented with acute right upper quadrant pain and jaundice. He was ruled out for Hepatitis A, B, C, HIV and for Tylenol overdose. Denied alcohol abuse. Total bilirubin from 10 to 17, direct bilirubin from 6.5 to 11 and alkaline phosphates from 350 to 636. Jaundice was consistent with obstructive pattern. Ultrasound abdomen-sludge in gall bladder, no stones or dilatation of common bile duct (CBD). CT-dilated gall bladder, no pancreatic mass. AFP-3, CEA-3.2, CA 19-9(437452 U/mL, (Normal <37 U/mL), PTCA revealed filling defect in distal CBD possible stone or stricture. He underwent exploratory laparotomy, cholecystectomy, CBD exploration, choledochoscopy and pancreatic head biopsy. CA 19-9 decreased to 1856 and then to 205 U/mL. Biopsy revealed fibrosis of peripancreatic tissue and chronic inflammation of CBD, gall bladder. Pancreatic malignancy and cholangiocarcinoma were ruled out. Although CA 19-9 was markedly elevated, further evaluation showed it was due to benign stricture.

**CONCLUSION:** CA 19-9 may be elevated in both benign as well as malignant conditions and interpretation of CA 19-9 results must be made in light of clinical condition.

**Hyperthyroidism as the Cause of Cholestatic Liver Disease.** C. Castillo, M. Sethi, and R. Rojas. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**CASE:** A 47-year-old male who presents with one month history of jaundice, generalized pruritus, trouble sleeping, tremors, weight loss (30 lbs.), diarrhea and abdominal pain. Past medical history is not relevant. Social history of alcoholism, last alcohol intake one year before admission. Alkaline phosphatase 309 IU/L, ALT 112 IU/L, AST 161 IU/L, bilirubin direct 1.0 mg/dl and bilirubin total 1.4 mg/dL. Renal function is normal. Abdominal ultrasound, CT scan of abdomen, and MRCP are unremarkable. Hepatitis profile, HIV test, ANA, antimitochondrial antibody and antismooth antibody are negative. There is no heart failure. Thyroid function test: TSH: 0.02 UIU/mL, T4: 19.80 UG/dL, T3: 411.7 ng/dL. The patient was treated with iodine I-131: (20.9 mCi) orally. Two months later liver function tests are almost back to normal, the patient is gaining weight and admits to being asymptomatic.

**DISCUSSION:** One of the many hepatic functions is the metabolism of the thyroid hormones. Therefore, it can be expected that the alterations of thyroid hormones influence hepatic function with different intensity, depending on the individual characteristic (in the case history of alcohol abuse). This case emphasizes that hyperthyroidism should be considered in the differential diagnosis of cholestasis.

**An Unusual Presentation of a Common AIDS Related Condition.** M. Fernandez<sup>1</sup>, C. Castillo<sup>1</sup>, A. Grigoriu<sup>1</sup>, D. Flores<sup>1</sup>, C. Strand<sup>2</sup>; U. Pai<sup>2</sup>, and H. Upadhyaya<sup>1</sup>. Departments of <sup>1</sup>Medicine and <sup>2</sup>Pathology. Jersey City Medical Center, Jersey City, NJ.

**INTRODUCTION:** Kaposi's Sarcoma (KS) is a malignant skin lesion seen before 1980 in elderly white men and now in homosexual men with AIDS. The Human Herpes virus 8 (HHV-8) is universally present in all forms of KS.

**CASE:** A 36-year-old male presented to Infection Disease Clinic with swelling, tenderness, and redness of the right knee. He had a history of HIV/AIDS, CS4 (40) viral load of 191,250 copies and noncompliance with highly active antiretroviral treatment (HAART) medications. He also had a history of oral thrush, MAI and chronic pancreatitis. He denied prior history of knee trauma, no sexual relations, no IV drug use, no history of gout, Lupus or rheumatoid arthritis. Vitals were blood pressure 125/72, P 82, RR

18, T 98.&. Right knee showed swelling, redness and mild limitation of movement; the rest of the exam was normal. X-ray of right knee showed only degenerative changes; a venous Doppler was negative for deep vein thrombosis (DVT), but revealed external compression of right popliteal vein due to cutaneous inflammatory lesions. He received Ultram for pain and HAART medications. One week later the patient came back with more pain in the right knee and described a tingling, burning sensation starting from the right groin area, coming down to the calf. There were vesicular lesions of the right medial knee in a dermatomal pattern. Valtrex was given and a few days later the lesions were transformed to furunculated masses that spread to the groins area. The leg was very swollen; he was not able to walk and was sent to the hospital. Surgical biopsy of the lesion revealed KS, and the patient improved rapidly with chemotherapy.

**HIV 1 ITP in Hepatitis C.** P. Thiruvilwamala and A. Grigoriu. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**INTRODUCTION:** Immune thrombocytopenic purpura is seen in approximately 40% of HIV infection patients (HIV-1-ITP). Destruction of platelets mediated by antiplatelet antibodies and/or platelet bound immune complexes is also seen in hepatitis C infection.

**CASE:** 37-year-old woman with HIV and hepatitis C co-infection who presented with thrombocytopenia. Patient had multiple hospital admissions for symptoms of epistaxis, bleeding per rectum and skin petechiae. Her baseline platelet counts were 2K-5K. Diagnostic workup including bone marrow biopsy and antiplatelet antibody proved ITP. She failed several attempts of treatment with steroids, IV immunoglobulin and AntiD. Rituximab and splenectomy were deferred in view of poor outcome. In the past, this patient was also noncompliant with highly active antiretroviral treatment (HAART) medications, had an episode of PCP pneumonia, genital herpes and had a short course of Peginterferon for hepatitis C.

**DISCUSSION:** Recognition of ITP in HIV-hepatitis C co-infected patients is important. The autoimmune nature of the disease, associated with hepatitis C and advantage of HAART in improving platelet counts should be kept in mind in addition to the first line of treatment. Cause of secondary thrombocytopenia including medications and viral/bacterial infections are also significant.

**Miliary Tuberculosis as a Source of Puerperal Fever.** H.D. Park, D. Kim, X. Mdluli, and L. Tacsá. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**LEARNING OBJECTIVES:** (a) To distinguish fulminant form of miliary tuberculosis from other forms of acquired pneumonia. (b) To identify effective diagnostic approach to disseminated tuberculosis

**CASE:** A 34-year-old Indian female living in the U.S. for 9 years with no known prenatal care presented with fever and productive cough one day after pre-term delivery. Physical examination findings showed occasional rhonchi in the chest. Chest X-ray and CT scan revealed bilateral diffuse reticulonodular infiltration involving both lower lobes. Despite empiric antibiotics treatment for 9 days, there was no clinical improvement. All the cultures and HIV test were negative. PPD showed 20 mm of induration. Laboratory data showed chronic anemia and elevated alkaline phosphatase. Liver, transbronchial and bone marrow biopsies revealed necrotizing and non-necrotizing granulomas that were consistent with disseminated tuberculosis. The condition of the patient has improved after starting anti-tuberculosis treatment. The patient was discharged on the 36<sup>th</sup> post-delivery day.

**DISCUSSION:** Miliary tuberculosis is an important differential diagnosis to the pneumonia patient who does not respond to conventional antibiotics, especially in the immigrant population group. Liver biopsy reveals highest yield among all the tissue diagnostic modalities in diagnosing disseminated tuberculosis.

**Streptococcus Pneumoniae Meningitis Presenting as Altered Mental Status.** Z. Awan, H. Moghaddam, A. Devarajan, and J. Matta. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**LEARNING OBJECTIVES:** (a) Consider *Streptococcus pneumoniae* as a caustic organism for meningitis in patients with altered mental status. (b) Even if the CSF is negative for any organisms, with positive blood cultures for *S. pneumoniae*, consider treating meningitis as due to *S. pneumoniae*.

**CASE:** A 57-year-old African-American female with h/o HTN evaluated for acute onset of altered mental status. Patient complained of severe headache with blurry vision the previous day and found to have drowsiness, lethargy, incoherent talk, feverishness, stiff neck, urinary incontinence without nausea and vomiting. Exam revealed an agitated, confused female, temp of 103°F, no neurology deficit except for a stiff neck, CT scan of head was negative, XCR was normal. Lumbar puncture revealed cloudy colorless CSF, glucose: 29; protein: 413, India ink -ve, WBC: 3650; (P-36, L-4), RBC: 4,200, gram stain and culture negative for any organism, bacterial antigen for *S. pneumoniae* +ve, CBC showed WBC 20.4, glucose 260, blood for gram stain showed G+ve cocci in chains and culture isolate *S. pneumoniae*. Patient was initially intubated for airway protection, treated with Pocephin and Dexamethasone. Patient regained full consciousness on the 3<sup>rd</sup> day and extubated.

**DISCUSSION:** Early consideration of *S. pneumoniae* meningitis with early institution of appropriate antibiotics and Dexamethasone results in rapid return of consciousness with no neurological sequelae. Even though CSF did not reveal organisms, isolation of organism in the blood is sufficient basis for effect treatment.

**The Effect of Intravenous Immunoglobulin (IVIG) in the Treatment of Toxic Epidermal Necrolysis.** Varadarajan, P. Venkataswamy, and R. Mikkilineni. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**INTRODUCTION:** Toxic epidermal necrolysis (TEN) is a severe cutaneous reaction mostly secondary to drugs, with high morbidity and mortality rate.

**CASE:** A 23-year-old Hispanic male was transferred to the hospital as he developed a diffuse rash all over his body. He developed sore throat about 3 days prior and took one unknown pill from a fellow inmate at 7 PM the previous night. At about 1 AM he noticed the rashes on his trunk, his face and then his extremities. It was getting worse over the day, accompanied by ulcers in the mouth and he was transferred to the ER. About 6 months prior, patient developed similar rash following penicillin ingestion and was hospitalized for 3 weeks with a diagnosis of Steven Johnson syndrome, for which he did not receive IVIG. On physical exam he was a moderately built male with polymorphic rashes ranging from small erythematous papules, palpable purpurae to 2–3 ringed target lesions, some with central vesicles were present all over the body, involving about 70% of the body surface area. We started him on IVIG within 24 hours of onset of rash and continued for 4 days. Over the next day the size of the lesions halted, but became more bullous and he had an episode of epistaxis with serosanguinous fluid. Nikolsky's sign was present. Patient felt significantly better earlier than the previous episode and was discharged in 10 days rather than 3 weeks.

**CONCLUSION:** Controversies still exist about the use of IVIG in the treatment of TEN. In our case, early administration of IVIG did significantly reduce the morbidity in terms of subjective symptoms and length of stay. IVIG may be beneficial compared to supportive care when administered early in the course of treatment of TEN.

**A 30-Year-Old Male with Single Ventricle Presenting with Bradyarrhythmia.** E. Bacorro, P. Thiruwilwamala, and J. Javed. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**INTRODUCTION:** Single ventricle is a rare congenital anomaly which presents at birth with cyanosis, congestive heart failure (CHF), or both. Palliative surgery is generally required early in life.

**CASE:** A 30-year-old male with history of diabetes mellitus, intravenous drug abuse (IVDA), and congenital heart disease (CHD) was brought to the ER due to chest pain, palpitations, dizziness and shortness of breath. Examination revealed an irregular heart rate, with systolic murmur at precordial area. EKG showed sinus rhythm, 1° AV block, and Q and ST changes in II, III, AVF. He had occasional junctional rhythm with the P waves on telemetry. Echocardiogram showed a single ventricle with a graft occluding the AV valve. He was transferred to CCU and stabilized. During childhood, he was diagnosed to have a single ventricle, LV type, with severe valvular and supravalvular pulmonary stenosis. At 18 years old, he had a modified Fontan-Kreutzer repair, with closure of the right atrioventricular valve and anastomosis of the main pulmonary artery to the roof of the right atrium. He was apparently well afterwards. However, since 2003, he had various admissions for CHF, atrial fibrillation/flutter, digoxin toxicity, and bacterial endocarditis.

**CONCLUSION:** Although patients with CHD are seen by pediatric cardiologists and surgeons, improvements and modifications in surgery have resulted in long-term survival and improve quality of life. Consequently, these patients are increasingly seen by adult medicine specialists. It is therefore important for internists to be familiar with the sequelae and associated complications of the surgical procedures, and the management of these conditions.

**Benefits of Thrombolytic Therapy in Massive Pulmonary Embolism.** E. Martinez, S. Titapiwatanakun, C. Onunkwo, M. Sethi, T. Borisiak, and D. Flores. Department of Medicine. Jersey City Medical Center, Jersey City, NJ.

**CASE:** A 32-year-old African-American male with history of complicated diabetes mellitus admitted with sudden onset of shortness of breath (SOB). Time since onset of symptoms to ER was 2 hrs. On admission patient was in severe respiratory distress – RR 40, diaphoretic, hemodynamically unstable (hypotensive, tachycardic, hypoxemic) that supported decision of intubation. Labs: D-dimer – 9.41, arterial pO<sub>2</sub> – 163 on 100% NR mask. CKMB – 4.6, trop – 0.5. Patient was administered levothep, insulin and heparin ggt. Lower extremity venous US showed CVT in left common femoral and popliteal veins. ECHO – decreased RVF, dilated, RV. V/Q scan – massive left lung pulmonary embolus with no perfusion. Decision was made to administer TPA 100 mg. Without change in heparin ggt (PTT 2 1/2 NL value). In less than 12 hours after TPS administration patient regained hemodynamical stability, arterial PO<sub>2</sub> normalized and follow-up V/Q scan showed completed resolution of pulmonary embolism.

**DISCUSSION:** Right-sided heart failure and recurrent pulmonary embolism are the main cause of death associated with pulmonary embolism in the first two weeks after the embolic event. Indications for thrombolysis are not well defined and thus controversial. The only current absolute indication is massive pulmonary embolism with hypotension, which was the clinical scenario with our patient. Other potential indications include right heart dysfunction, recurrent pulmonary embolism and the prevention of pulmonary hypertension. However, no evidence exists to show benefit of thrombolytic therapy over standard anticoagulation therapy for recurrent pulmonary embolism, mortality or chronic complications. Bleeding is the most common complication of thrombolysis and may be fatal.

## Queens Hospital Center

**When Wheezing Is Not Due to Asthma.** K. Amaechi, E. Okundaye, D. Reich, and R Lopez. Queens Hospital Center, Mount Sinai Services, Jamaica, NY.

We report the case of an elderly woman with multiple hospitalizations for illness, which in the past had been variously diagnosed as asthma, congestive heart failure, and pneumonia. The patient's symptomatology appeared not to fit into any one specific disease category in this, as in previous admissions. Her present illness proved to be another great mimicker in medicine and her response to a variety of treatments remained suboptimal until the proper diagnosis was made, given a careful clinical assessment of her illness.

**CASE REPORT:** PM is an 80-year-old woman who presented with complaints of shortness of breath and cough that produced clear sputum for two weeks with occasional bloody streaks. She had progressive shortness of breath, orthopnea and leg swelling, but denied fever. She had been diagnosed with late-onset asthma during a previous admission, had well-controlled diabetes, and never smoked nor used illicit drugs. She had retired from her job of making artificial hair for dolls 15 years earlier. Review of systems was significant for weight loss of 10 lbs over a one-month period. The patient's medications were fosinopril, metoprolol, rosiglitazone, furosemide, albuterol and ipratropium metered dose inhalers. Physical examination revealed an afebrile, dyspneic and wheezing woman. On auscultation, she had ronchi in both upper lung zones and crepitations in both lower zones. The extremities were significant for grade one, non-pitting pedal edema. The white blood cell count, serum chemistries and chest X-ray were normal, and two sets of blood cultures were did not grow any organisms after five days.

Her present illness was treated as an exacerbation of asthma and chronic heart failure. While this patient was receiving nebulizers and diuretics her pedal edema improved, however, she continued to feel

generally weak and she deteriorated despite therapy, with persistent cough and shortness of breath. An echocardiogram was subsequently obtained, which revealed a left ventricular hypertrophy, a normal ejection fraction, a Tajik grade one diastolic dysfunction and a pulmonary artery systolic pressure of 33 mmHg. The echocardiographic findings failed to account fully for the patient's collection of signs and symptoms, and some other pulmonary etiology was suspected.

At this point, the dose of diuretics was gradually reduced, and further testing pursued. Pulmonary function tests (PFT) and high-resolution computed tomography (HRCT) of the chest were obtained. The PFT study was limited due to poor patient effort and fatigue, however data obtained was sufficient to suggest a restrictive ventilatory defect. HRCT of the chest revealed bilateral bronchiectasis with extensive fibrotic changes in the lung bases. In the light of this finding antibiotics were then added to the treatment regimen, and the patient demonstrated marked improvement of her symptoms.

**DISCUSSION:** Bronchiectasis is defined as an abnormal and permanent dilatation of bronchi and bronchioles. The diagnosis requires a high clinical suspicion and the gold standard for its diagnosis is a HRCT. Patients with bronchiectasis frequently have recurrent infections, with increased secretions that can harbor pathogens. Inflammatory mediators are released, and these together with bacterial activity lead to destructive changes in the bronchial wall, squamous metaplasia, and increased vascularity of the bronchial vessels culminating in fibrous tissue replacement. Common causes include pneumonia, TB, HIV, endobronchial tumors, cigarette smoking, recurrent gastric aspiration, hereditary syndromes such as Kartagener's syndrome, cystic fibrosis, and some cases are idiopathic, having no known underlying cause.

Signs include adventitious breath sounds in virtually all patients, crepitations are present in 70%, wheezing in 34% and ronchi in 44%. In the past, digital clubbing was a frequent feature but a recent series describes a prevalence of only about 3%. Furthermore, fever, non-specific weight loss and anemia are frequently present among patients.

Treatment is focused on treating the underlying cause(s). Infections are usually treated empirically with antibiotics and recent studies have focused on aerosolized aminoglycosides which can reduce colonization by pseudomonas as in cystic fibrosis patients. Albuterol is the bronchodilator of choice and enhances mucociliary clearance. The benefits of chest physiotherapy, mucolytic agents, and postural drainage has not been established. Surgery is indicated for focal lesions with massive hemoptysis when conservative treatment fails. Angiographic embolization can be of use in selected cases.

**CONCLUSION:** Bronchiectasis is a disease with variable etiologies and clinical manifestations not truly typical of any one specific disease process. Despite our patient's wheeze, she did not improve with therapy for asthma. While her slight pedal edema improved with diuresis, her shortness of breath, cough and basilar crepitations did not improve until antibiotics were added following HRCT. Future treatments will be focused on primary prevention and localization of antibiotic delivery.

**Neurosarcoidosis—A Diagnostic Difficulty.** M.J. Bhutta (PGY 2), D. Modi and Intazam-u-Khan. Departments of Medicine and Neurology. Mount Sinai School of Medicine at Queens Hospital Center, Jamaica, NY.

**INTRODUCTION:** Neurosarcoidosis is an uncommon but serious, sometimes life-threatening manifestation of sarcoidosis. The diagnosis of neurosarcoidosis is often difficult, particularly in patients who lack either pulmonary or systemic manifestations. Neurologic sarcoid occurs in fewer than 10% of patients with sarcoidosis. We report a case with neurological manifestations as a sole presentation of sarcoidosis.

**CASE REPORT:** A 44-year-old woman from Trinidad with no significant medical history presented to the emergency department complaining of lightheadedness, nausea, increasing difficulty walking and occasional vomiting for 3 days. Except for transient occasional double vision for 2–3 years, she denied fever, headache, recent viral illness, polyuria, polydipsia, tinnitus, hearing loss, ear pain, blurring of vision, vertigo, syncope or any menstrual irregularities. She also denied smoking, using alcohol or drugs and sexual promiscuity.

On examination she was not orthostatic. Neurologically she was alert and oriented. She had fluent speech with no anxious mood. Cranial nerve examination showed pupils 2–3 mm bilaterally equally reactive to light and accommodation. There was horizontal nystagmus with the fast phase towards the left side and good visual fixation. No other cranial nerve abnormalities were noted. The motor system was significant for spasticity in all four extremities, 3+ deep tendon reflexes

and bilateral ankle clonus. Co-ordination showed intentional tremors, difficulty walking, spastic and ataxic gait, positive romberg's sign and difficulty in tandem walking. Finger to nose and heel to shin test were normal. There were no sensory abnormalities noted. Other systemic physical examination was essentially normal.

Initial laboratory studies including routine serum chemistries and liver function tests showed no significant abnormalities. Chest X-ray and a non-contrast CT scan of the head were within normal limits. Lumbar puncture revealed clear cerebrospinal fluid, normal opening pressure of 90 cm H<sub>2</sub>O, leukocytosis (WBC 23/cumm, normal: 0–5) and significant lymphocytosis 98% (40–80%). Low glucose 33 (40–80) and very high protein 214 (15–45) were noted in the cerebrospinal fluid. Neurology and infectious disease consults were requested. Serious consideration was given to tuberculous meningitis, CNS demyelinating disease, carcinomatous process, Lyme's disease, sarcoidosis, human T lymphotropic virus, human immunodeficiency virus or Herpes simplex virus infections. MRI with gadolinium showed diffuse leptomeningeal enhancement along the basilar, interpedicular and supra sellar cisterns and anterior to the pons and quadrigeminal spaces. Marked dural thickening of the cervicomedullary junction extending to the left cerebello-pontine angle was also noted, strongly suggesting neurosarcoidosis. Tuberculous meningitis and eosinophilic granuloma could not be ruled out. The patient was treated with high-dose intravenous pulse methylprednisone. There was a dramatic clinical response over 2–3 days. CT of the chest was suspicious for sarcoidosis. A transbronchial biopsy from right upper lobe did not show sarcoidosis. A surgical consultant performed a biopsy of the right para tracheal lymph node via mediastinoscopy. The pathology report was non-caseating granuloma with negative stains for acid-fast bacilli and fungi. Other lab work-up showed normal levels of angiotensin-converting enzyme and vitamin D.

The patient was discharged after 2 weeks of clinical stability with steroid being tapered. She again presented to the emergency department two weeks later for a likely flare-up with similar but less intense manifestations, possibly secondary to the rapid steroid tapering. Her steroid dose was again increased with a good clinical response. The patient was discharged to be followed in the neurology clinic.

**DISCUSSION:** Neurosarcoidosis is a rare disease with many presentations. It can appear in an acute, explosive fashion or as a slow, chronic illness. It can manifest as cranial neuropathy, aseptic meningitis, mass lesions, encephalopathy, vasculopathy, seizures, psychiatric manifestations, hydrocephalus, hypothalamic pituitary disorders, myelopathy, peripheral neuropathy or myopathy. Our case was unique in terms of signs and symptoms suggesting cerebellar area of involvement. MRI of the head was markedly abnormal with enhancement especially along cisternal and subarachnoid spaces without any evidence of a mass lesion.

Unlike pulmonary sarcoidosis where a period of observation is recommended for mild and asymptomatic cases, neurosarcoidosis should always be promptly treated. Treatment decisions are governed by disease location, clinical severity, time course and possible morbidity of the treatment. Corticosteroids are the cornerstone of therapy for neuro-sarcoidosis. Steroid therapy is usually started at a high dose and after a clinical response is achieved, the dose is gradually tapered. In patients where corticosteroids may be contraindicated, cytotoxic drugs such as methotrexate, azathioprine, cyclosporin, and cyclophosphamide have been used. Immunomodulators such as infliximab have been reported to be effective in a few cases with refractory sarcoidosis. Radiation therapy can also be used in patients who do not respond to drug therapy. Neurosurgical resection of intra cranial and spinal granulomas is only indicated in life-threatening situations or where medical treatment is insufficient.

**A 46-Year-Old Man with Superior Pulmonary Sulcus Tumor and Pancoast Syndrome.** O.I. Constantine and P. Rekha. Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

**INTRODUCTION:** Shoulder and arm pain from a superior sulcus tumor is a commonly misdiagnosed sign of lung cancer. The pain results from local extension of a tumor in the apex of the lung, with involvement of the eighth cervical and first thoracic nerves. Unfortunately, shoulder and arm pain are often mistaken for arthritis or bursitis of the shoulder, or cervical osteoarthritis.

**PRESENTATION OF CASE:** A 46-year-old man with no medical history was referred to the medical clinic eleven weeks after his third emergency room visit because of right shoulder pain. The shoulder pain was worse with movement and was associated with mild numbness in the right hand. He also had a 4-month history of a burning sensation

over the skin of the right shoulder and painful swelling of the right anterior chest wall. He denied fever, trauma, cough with sputum production, dyspnea, hoarseness, fever, chills, sweats, exposure to industrial dusts or carcinogens or weight loss. He had no surgical history and no allergies. He emigrated from Jamaica, West Indies and has a 20-pack-year history of tobacco use. He denied drug use and drank alcohol occasionally. He was unemployed.

His systems were negative for fever, night sweats, weight change, headache. He admitted to not sweating on the right side of the face in the last year. He denied shortness of breath, orthopnea, paroxysmal nocturnal dyspnea, ankle swelling, dysphagia, nausea, vomiting, diarrhea, change in bowel movements or bone pains other than the right shoulder pain.

His vital signs were normal: BP 130/80 mmHg, pulse 80/min, respiration 12/min, temperature 98°F. On examination, the patient appeared well developed and well nourished. He had anicteric sclerae, pink conjunctivae and a moist buccal membrane. He had no palpable cervical, supraclavicular or axillary lymphadenopathy. There was no swelling and no tenderness of the shoulder joints but there was pain on performing movements at the right shoulder joint. He had no deformities and no paraspinal tenderness. The results of a neurologic examination were normal except for Horner's syndrome (ptosis, miosis, and anhydrosis) of the right eye. There was a tender, immobile, 2 × 2 centimetres upper right-sided diffuse swelling of the anterior chest wall. The lungs were clear to auscultation, his heart and abdominal examination revealed no abnormalities. He had no costovertebral angle tenderness. There was no peripheral edema or digital clubbing.

Microscopic examination of two CT scan-guided fine-needle aspiration biopsies of a 7 cm variegated mass involving the right apex revealed a poorly differentiated squamous cell carcinoma. CT scan of the brain without contrast was normal. Total body bone scan showed no evidence of skeletal metastasis. Echocardiography, renal and abdominal ultrasound studies were normal.

The diagnosis of a limited stage poorly differentiated non-small cell lung cancer stage 11B was made and the patient was treated with a course of concurrent radiation therapy and weekly Taxol and carboplatin. Over time, the patient showed clinical and radiologic evidence for local and metastatic relapse involving the brain and lumbar spine. He received external beam radiation to his brain with improvement. His lung cancer continued to progress and no further chemotherapy was recommended.

**DISCUSSION:** Pancoast's description of the clinical and radiologic features, which led to the eponym, was published in 1924. The symptoms of the Pancoast syndrome include pain in the ipsilateral shoulder and arm along the distribution of the trunks of the eight cervical and first and second thoracic nerves, Horner's syndrome, and weakness and atrophy of the hand muscles. Phrenic nerve or recurrent laryngeal nerve involvement, the superior vena cava syndrome, and supraclavicular lymph node disease are less common.

Pancoast's syndrome may be the result of diverse neoplastic, inflammatory or infectious diseases or neurogenic thoracic outlet syndromes such as the cervical rib, and pulmonary amyloid nodules. It is, therefore, necessary to make a definitive diagnosis prior to treatment. The majority of patients with Pancoast's syndrome have non-small-cell bronchogenic carcinoma, most commonly squamous, followed by adenocarcinoma, although in several series adenocarcinoma was the most frequent histologic type. Small-cell carcinoma is only rarely associated with this syndrome.

Relapse in the form of local or regional occurrence of disease or distant metastasis are common after the treatment of superior sulcus tumors. Brain metastasis is one of the most common forms of disease progression, especially with poorly differentiated large-cell carcinoma and adenocarcinoma. Hence, some authors recommend prophylactic cranial irradiation for these patients. Because of the peripheral location of the tumors that cause the Pancoast syndrome, patients rarely present with cough, hemoptysis, or dyspnea and hence are not diagnosed early. They are often initially treated for arthritis or bursitis of the shoulder, or cervical osteoarthritis. Pancoast tumor should be considered in the differential diagnosis of shoulder pain.

**Nafcillin-Associated Hypokalemia—A Case Report.** M. Gill, H. Gill, N. Gill, and I. Sachmechi. Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

**INTRODUCTION:** A low-serum potassium concentration is one of the most common electrolyte abnormalities encountered in clinical practice. Even mild or moderate hypokalemia increases the risks of morbidity and mortality in patients with cardiovascular disease. As a result, when hypokalemia is identified, the underlying cause must be sought

and the disorder treated. Antibiotics, which are the most commonly prescribed therapeutic agents in hospital, are one cause of hypokalemia that is often overlooked. We present a case of hypokalemia secondary to high dose nafcillin therapy.

**CASE REPORT:** A 46-year-old normotensive, diet controlled diabetic African-American man presented to the emergency department with right flank pain of four days duration. Associated symptoms were dysuria, anorexia, weight loss, generalized weakness and back pain for about a month. On physical examination his vital signs were: blood pressure: 116/78 mm Hg, pulse rate: 88/min, respiratory rate: 18, temperature: 99.2°F. The rest of the physical examination was significant for a 6cms fluctuant non-tender submandibular swelling, left-sided pleural effusion and tenderness over the right costovertebral angle. The aspirated pleural fluid was consistent with empyema, and together with blood cultures, grew methicillin-sensitive *Staphylococcus aureus*. Transesophageal echocardiography did not reveal any valvular vegetations. There was evidence of osteomyelitis of the T12–L1 vertebrae. His submandibular swelling was drained of purulent material and his empyema required chest tube drainage. The patient was treated with intravenous nafcillin, followed by considerable clinical improvement. His hospital stay was complicated by severe and resistant hypokalemia, which remained uncorrected even with supplementation of up to 240 meq of potassium chloride every day. No non-renal cause to account for the hypokalemia was found, except that the patient had evidence of renal potassium wasting with urine potassium of 37.6 meq/L. At this point, nafcillin was replaced with vancomycin, with gradual return of his potassium levels to normal over the next two weeks without necessitating potassium supplementation. It was concluded that nafcillin resulted in potassium wasting, which resolved after the drug was discontinued.

**DISCUSSION:** Nafcillin is a very useful penicillinase-resistant antibiotic, commonly used in clinical practice. It also may have protean adverse drug manifestations such as high-dose nafcillin (>4 gm/day)-associated hypokalemia, by promoting renal potassium excretion due to increased sodium delivery to the distal nephron. This abnormality gradually reverses after the drug is discontinued or dosage is decreased.

**CONCLUSION:** The differential diagnosis of any patient with hypokalemia should include medications, especially drugs with high sodium content. This knowledge may save an otherwise extensive work-up for hypokalemia.

**Life-Threatening Angioedema in SLE—A Case Report.** H. Gill, M. Mutic, M. Gill, S. Kucinska, and A. Opran. Department of Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

**INTRODUCTION:** Systemic lupus erythematosus (SLE) can have protean manifestations involving virtually any organ system in the body. Life-threatening angioedema involving the upper respiratory tract is an unusual manifestation of SLE. We report a case of a 45-year-old Hispanic man who developed supraglottic edema causing airway obstruction requiring tracheostomy and mechanical ventilation, as well as treatment with high-dose IV steroids during the active disease process.

**CASE REPORT:** A 45-year-old Hispanic man with history of SLE presented to the Emergency Department (ED) with one-day history of fever, sore throat, dysphagia and difficulty in breathing. He had pain and swelling of the knees and ankles for two months. He denied prior cough, sputum, pleuritic chest pain or similar illness, although he had been hospitalized several times for SLE flares. His vital signs in the ED were: blood pressure 153/94 mm Hg, temperature 97.1°F, pulse 88/min, respiratory rate 20/min, and O<sub>2</sub>-saturation of 98%. On examination, he had tongue swelling and inflammation of his knees and ankles. Otorhinolaryngologist was consulted and fibro optic nasopharyngeal laryngoscopy showed swelling of his tongue and uvula, supraglottic edema and airway obstruction. The patient was intubated and placed on mechanical ventilation. He also received high-dose intravenous steroids. Five days later, laryngoscopy showed complete resolution of supraglottic edema, biopsy of uvula and posterior pharynx was performed, and the tracheostomy was closed. Laboratory testing revealed a normal C1-inhibitor (C1-INH) level and increased lupus activity, evident by increased levels of CRP, anti-ds DNA, and decreased levels of C3 and C4. After an extra week in the rehabilitation department, the patient was discharged home.

**DISCUSSION:** Angioedema is a condition characterized by the extravasation of fluid and its entry into interstitial tissues. It results from the release of inflammatory mediators that facilitate dilation and enhance the permeability of capillaries and venules. It is a rare occurrence in SLE and its mechanisms are heterogeneous. SLE can be associated with hereditary and acquired deficiencies of C1-INH or dysfunctional

C1-INH. Our patient did not have a personal or family history of angioedema and/or urticaria and his C1-Inhibitor level was within the normal range. He was not taking an ACE inhibitor or other medications known to have a potential to cause angioedema. He presented with a 2-day history of fever, odynophagia and sore throat and his lupus activity was increased as evidenced by arthritis of his knees and ankles, increasing levels of CRP and anti-dsDNA, and decreased levels of C3 and C4. Therefore, we suggest that it might have been an upper respiratory infection in the presence of active SLE that precipitated his angioedema.

**CONCLUSION:** Angioedema in SLE is a potentially fatal condition as the swelling of the tongue, uvula, soft palate, or larynx may compromise the airway. Timely securing of the airway and treatment of the underlying etiology ensure good outcomes.

**Diltiazem as a Treatment for Soft Tissue Calcinosis in Adult Onset Dermatomyositis.** G. Gupta, G. Mansouri, and A. Opran. Department of Internal Medicine, Mount Sinai School of Medicine, Queens Hospital Center, Jamaica, NY.

**INTRODUCTION:** Calcinosis, an accumulation of calcium hydroxyapatite, is often associated with dermatomyositis. Presentation of cutaneous calcinosis may range from hard painful nodular areas to stiffened areas in skin, cutaneous ulcer, joint contractures and muscle atrophy. Calcinosis associated with a connective tissue disorder is thought to be a localized process rather than a systemic disturbance in calcium homeostasis. A possible mechanism in dermatomyositis is release of mitochondrial calcium from cells into damaged muscle, which then forms a focus for dystrophic calcification. The calcinosis is very refractory in spite of treatment of the dermatomyositis, including the use of steroids and cytotoxic agents. Various calcium channel blockers have been tried to treat calcinosis but only diltiazem has been shown to be effective for calcinosis in juvenile onset dermatomyositis. We report a case of adult onset dermatomyositis with calcinosis, treated with diltiazem, who had a significant clinical improvement of the calcinosis.

**CASE REPORT:** A 55-year-old woman with active dermatomyositis presented with a 3-week history of generalized weakness and myalgia of limbs, muscle stiffness and worsening of rashes around the periorbital areas. Physical examination was positive for fever. Diffuse flat erythema in a shawl-like distribution was observed over the thorax and shoulders, in a V-shaped distribution over the anterior neck and chest, over the forehead, malar region and chin with a heliotrope rash on the upper eyelids accompanied by swelling of the eyelid. A violaceous erythematous rash was present over the extensor surfaces of the patient's metacarpophalangeal and interphalangeal joints of the fingers. She also had multiple tender, hard nodular lesions on both anterolateral areas of the thigh, right arm and sacral areas.

Laboratory findings were consistent with active dermatomyositis with a serum ANA titer of 1:1280, the creatinine kinase was increased to 1194 units/L. Radiographic analysis of pelvic and leg areas showed subcutaneous ossification/calcification in the soft tissue of the thigh. Bone densitometry showed increased bone mineral density in the femoral areas. The patient was receiving prednisone 10 mg orally once a day before hospitalization. This medication was changed to methylsuccinate prednisone 60 mg via intravenous route during the hospitalization. High-dose steroid therapy together with methotrexate and hydroxychloroquine treatment resulted in significant improvement in symptoms except around the calcific nodular areas, which were still painful. The patient was started on diltiazem for calcinosis, which resulted in significant improvement in pain around the areas of calcinosis and clinical improvement of the skin lesions.

**CONCLUSION:** Previous drugs used to treat ectopic calcification have included bisphosphonates, probenecid, aluminium hydroxide, warfarin and the local injections of glucocorticoids. Unfortunately, none have shown more than anecdotal success. The finding in our patient that long-term treatment with diltiazem resulted in significant improvement in calcinosis suggests that diltiazem, an L-type calcium channel blocker may offer more consistent therapeutic benefit.

**Case Report: Adult Intussusception.** Y. Hiltzik MS IV (NYCOM), R.A. Paguia, F. Wibowo, L. Kasturi, and A. Moskowitz. Department of Medicine, Mount Sinai School of Medicine/Queens Hospital Center, Jamaica, NY.

Intussusception is the invagination of a segment of bowel into the lumen of an immediately adjacent segment of bowel. The intussusceptum is the proximal segment of the bowel that prolapses into the distal adjacent segment, which is called the intussusciptens. Intussusception

occurs most commonly in children, accounting for most cases of intestinal obstruction. In adults, however, it is very rare, but when present, a cause is frequently identified in up to 90% of cases.

We report the case of a 48-year-old woman who presented with a 2-week history of intermittent, colicky, epigastric pain with accompanying nausea associated with oral intake but no vomiting. Symptoms resolved spontaneously. No bleeding per rectum or change in bowel habits or caliber of stool was reported. Last bowel movement was 4 days prior to hospitalization. The patient's medical history includes diabetes, hypertension, hyperlipidemia and esophageal reflux. The patient had 2 prior caesarean sections. There was no history of alcohol, tobacco or drug use. Home medications consist of insulin, pioglitazone, metformin, hydrochlorothiazide, gabapentin (for neuropathy secondary to diabetes) and fosinopril. Family medical history was notable for hypertension and diabetes. On examination, the patient appeared comfortable, with a blood pressure of 186/68 mm Hg, pulse rate of 100 beats per minute and respiratory rate of 12 breaths per minute. Patient was afebrile. Lungs were clear and there were no murmurs or extra heart sounds on auscultation. The patient was noted to have an obese soft abdomen but with direct tenderness over the epigastric and right upper quadrant areas, with no rebound or guarding; no masses or organomegaly were felt. Digital rectal exam showed external hemorrhoids, normal tone, no masses and heme negative stools. Apart from slight anemia, the patient's routine laboratory studies were unremarkable. Chest X-ray revealed only minimal cardiomegaly. Abdominopelvic CT scan showed colo-colonic intussusception at the level of the transverse colon. Colonoscopy done to evaluate the intussusception revealed an ulcerated villous adenoma tethered to the bowel wall at the mid transverse colon region. The patient subsequently underwent right hemicolectomy with no complications. Postoperative course was uneventful, and the patient went home on postoperative day five.

Intussusception in adults is a rare phenomenon; 85–90% of intussusception occurs during childhood, where it is the leading cause of bowel obstruction. The cause is not established, although it is believed that hypertrophy of Peyer's patches in the terminal ileum acts as the pathologic lead point in causing the invagination of the bowel segments. By contrast, adult intussusception has an identifiable cause in 90% of cases, mostly a neoplasm in the colon rather than in the small bowel. Other causes include postoperative adhesions, diverticuli, sprue, and HIV disease. The clinical presentation can be variable; often patients present with a chronic intermittent pain pattern that suggests chronic subacute intermittent partial bowel obstruction. Surgical resection is the definitive treatment in most cases due to the high incidence of malignancy.

**Severe Progressive Halothane Hepatitis with Remarkable Resolution after Treatment with Steroids.** S. Parab, S. Siripurapu, M. Shulimovich MS III (NYCOM), and E. Restrepo. Department of Medicine, Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

**INTRODUCTION:** Halothane is an inhalational anesthetic, commonly used worldwide, which may cause idiosyncratic reactions in adults, leading to hepatotoxicity. The resulting liver injury may vary in severity from a mild hepatitis without complications to severe fulminant hepatitis with hepatic failure leading to death. This type of liver damage has clinical, serological and immunological features compatible with an immune-mediated reaction. The treatment of halothane hepatitis is mainly supportive. The use of corticosteroids in this setting remains controversial, given the lack of controlled studies in the literature to support its use.

This case report describes a patient who developed symptomatic hepatitis following exposure to halothane, with progressive gradual clinical deterioration. The patient showed a rapid and sustained improvement following initiation of therapy with prednisone.

**CASE REPORT:** A 58-year-old woman from Guatemala with a medical history of gastroesophageal reflux disease (GERD) and chronic sinusitis presented to the emergency department with complaints of fever with chills, generalized body ache and weakness for two days, and nausea, vomiting and diarrhea for one day. Ten days earlier, she had undergone sinus surgery (recannulation) under general anesthesia in Guatemala without any complications. After surgery she was prescribed a non-steroidal anti-inflammatory (NSAID) as well as a quinolone antibiotic for seven days. She was doing well when she travelled to New York 5 days after surgery. On the 6th day, she developed the above-mentioned symptoms. The patient was taking only acetaminophen 650 mg every four hours for two days prior to admission, to ease her pain and fever.

In the ER, her blood pressure was 80/40 mm Hg, pulse 117 bpm, respiratory rate 20 breaths per minute and temperature 100.8° F. Phys-

ical examination was significant for slight jaundice, right upper quadrant abdominal tenderness, and some maxillary tenderness.

The initial laboratory tests revealed a serum aspartate transaminase (AST) of 1159 units/L, serum alanine transaminase (ALT) of 1,049 units/L, total bilirubin 3.5 mg/dL, alkaline phosphatase 152 units/L. The white blood cell count was 13,600/mL with 70% neutrophils, 14% bands and 4% eosinophils. The prothrombin time was prolonged, at 19.8 seconds (INR 2.58), and partial thromboplastin time was 36.1 seconds. Chest X-ray revealed no abnormalities. Abdominal ultrasound was unremarkable except for a small cyst in the upper pole of the right kidney. Hepatitis A, B and C serologies as well as leptospira antibodies were negative. Acetaminophen level was less than 10 mcg/mL and serum ANA titer was negative.

By the tenth hospital day, anorexia, nausea and vomiting persisted, and the patient was markedly jaundiced and experienced periods of mild confusion despite treatment with lactulose. On repeat blood tests, the AST peaked at 2,256 units/L, ALT at 1,176 units/L, total bilirubin rose to 23.1 mg/dL and eosinophilia increased to 17% (absolute eosinophil count 1,768/mL). CT of the abdomen showed common bile duct dilatation and a questionable duct stone. Subsequently the patient underwent an unsuccessful endoscopic retrograde cholangiopancreatography (ERCP), followed by magnetic resonance cholangiopancreatography (MRCP), which confirmed the dilation of the common bile duct.

Additional information was obtained from Guatemala. The patient had received the anesthetic halothane during her recent sinus surgery. At this point, the diagnosis of halothane-induced hepatotoxicity was strongly considered. In view of the patient's progressive clinical deterioration while receiving supportive treatment, and the unpredictable course of halothane-induced hepatitis the patient was given a trial of corticosteroids. Treatment with a tapering course of prednisone starting with 60 mg daily was given over the course of two weeks. On the 3rd day of prednisone therapy the patient reported feeling significantly better with complete resolution of nausea and vomiting, and improved appetite. The liver function tests also showed marked improvement and the jaundice promptly cleared. Follow-up abdominal ultrasound performed 12 days after starting prednisone revealed resolution of the common bile duct dilatation. Four months after hospital discharge the patient reported feeling well.

**DISCUSSION:** The clinical diagnosis of halothane-induced hepatitis was made in this patient. Ten days after receiving halothane anesthesia, she developed the characteristic clinical picture of fever, anorexia, nausea, myalgias, jaundice, marked elevation of serum transaminases and eosinophilia. In addition, there was no evidence for viral, autoimmune or metabolic causes of hepatitis. Halothane hepatitis is due to hepatocellular damage caused by an immune response directed against hepatocytes with trifluoroacetate (TFA) protein adducts. TFA (trifluoroacetate) is a metabolite of halothane, which binds to hepatocyte macromolecules and phospholipids producing TFA-protein adducts which act as sensitizing neoantigens leading to fulminant hepatic necrosis.

Although the general consensus in the management of halothane hepatitis is supportive therapy, the fact that halothane-induced hepatotoxicity constitutes an immune-mediated idiosyncratic reaction with an unpredictable course including fulminant hepatitis and even death, a trial with prednisone should be considered in patients who have evidence of severe halothane-induced liver injury such as the case presented here. Therapy with prednisone appears to decrease morbidity and hasten the resolution of the immune process. In the U.S., halothane has not been used in adults since 1970s. However, it continues to be used commonly in other countries and should be considered in the differential diagnosis in an immigrant patient presenting with liver dysfunction in the postoperative period.

**A Walk in the Desert: Corticosteroids in Disseminated Coccidioidomycosis.** N. Popovic, R. López. Mount Sinai Services at Queens Hospital Center, Jamaica, NY.

LR was a 28-year-old Spanish-speaking man from Guatemala who entered the U.S. five months prior to presentation by walking from Mexico across the Arizona desert three times. He complained of loss of appetite and a 50 lb weight loss over 2 months, cough productive of whitish sputum, loose stool without mucus or blood, and subjective fever for one month. He denied using drugs, smoking cigarettes, or using alcohol; he also denied risk factors for HIV or TB exposure. The patient had no previous medical problems and did not take medications.

On examination the patient was cachectic, blood pressure was 102/62 mmHg, heart rate was 142 bpm and he had a fever of 103° F. Respiratory rate was 20. He had coarse breath sounds with crackles more prominent in the left lung field. His inguinal lymph nodes were enlarged without induration. The remainder of his physical examination was normal. Laboratory data revealed a normocytic anemia with a normal white blood cell and differential counts; serum chemistries revealed sodium 124, potassium 2.5, chloride 91, glucose 146 and calcium 7.5. His chest X-ray revealed patchy bilateral infiltrates.

The patient was hospitalized and treated for community-acquired pneumonia. He continued to have daily fevers ( $T_{max}$  104.2° F), and his bowel movements remained loose. Anemia work-up was consistent with the anemia of chronic disease. CT of his chest revealed extensive parenchymal consolidation in the upper lobes associated with numerous acinar nodules and extensive mediastinal and left hilar adenopathy as well as bilateral pleural effusions. A CD4 count was 51 cu/mm, CD4/CD8=0.08. Empiric therapy for *Pneumocystis carinii* pneumonia and TB were added to his treatment. The patient was transferred to the ICU because of hypotension (BP was 80/54 mm Hg) that responded to aggressive fluid replacement. A bone marrow aspiration and biopsy was non-diagnostic. Bronchoalveolar lavage revealed negative smears for *P. carinii*, acid-fast bacilli and fungus. Transbronchial biopsy revealed unremarkable lung with no granuloma. Ophthalmology consultation revealed small, flat, white lesions, which were felt to be nonspecific findings. The patient was intubated and started on pressor drugs for hypotension (BP was 70/50 mmHg) and tachypnea. A random cortisol level was 9.93 U $\mu$ g/dL; hydrocortisone was given for presumed adrenal insufficiency. Blood cultures were reported to show gram positive cocci in clusters and vancomycin and empiric amphotericin B was added to this treatment regimen. The patient steadily deteriorated and met the criteria for acute respiratory distress syndrome; he later developed a tension pneumothorax which was emergently decompressed with angiocatheter. Right 18 French Chest tube was placed in the right lung.

The blood cultures previously reported to contain gram positive cocci in clusters were corrected and were than reported to be growing mold. No changes were made in management. The patient expired shortly thereafter.

Postmortem laboratory coccidioidomycosis results included all blood cultures growing fungus. Bronchoalveolar lavage and transbronchial biopsy cultures were negative for acid-fast bacilli. Transbronchial biopsy grew *Coccidioides immitis*. His bone marrow biopsy was negative for fungus.

**CONCLUSION:** The definitive diagnosis may be made too late to save the patient, as there is no reliable rapid testing method to diagnose this condition. Despite the fact that *C. immitis* is capable of growing in bacterial blood culture media, it is a lengthy process and can be mistaken for gram positive bacteria as occurred in our case. However, diffuse pneumonia with a reticulonodular pattern in a patient with an appropriate travel history should serve as a clue to raise the index of suspicion to consider coccidioidomycosis as a diagnosis.

Most *Coccidioides* infections do not require treatment, and those that do usually respond to antifungal therapy. Fulminant coccidioidomycosis is a more serious condition; a recent report of a case of fulminant coccidioidomycosis in an immunocompetent patient with severe acute respiratory distress syndrome stated that the use of corticosteroids in addition to standard antifungal treatment produced a good outcome. However, this observation does not seem to apply in our case and others. Contrary to the well-established use of corticosteroids in the treatment of PCP pneumonia and sepsis, use of corticosteroids in coccidioidomycosis is controversial. A retrospective study of immunocompromised patients with hematologic malignancy did not support the use of corticosteroids in the management of disseminated coccidioidomycosis.

Until 2004 only 11 cases of septic shock due to coccidioidomycosis were described without long-term survival. In November 2004 the first successful outcomes in patients with septic shock due to coccidioidomycosis were reported in immune competent patients. Two cases of septic shock associated with coccidioidomycosis that were successfully treated with *drotrecogin alfa* (activated) in combination with antifungal agents.

This reported case highlights the need for further investigation of the role of corticosteroids in respiratory failure due to coccidioidomycosis. It also highlights the impact that world travel imposes on physicians all over the world, who need to be ready to diagnose problems limited to small endemic areas in addition to the interrelations these problems may have with a growing population of immunocompromised patients.