Rhode Island Chapter, American College of Physicians 2010 Annual Meeting Abstracts

In May 2010, the Rhode Island Chapter, American College of Physicians, hosted its annual Associates' Forum Competition at the Crowne Plaza Hotel in Warwick. More than 110 residents in Rhode Island's teaching hospitals submitted entries. A committee of program directors chose the following six winners. These six podium presenters each received a plaque and a cash award from the College Chapter. The Chapter and program directors applaud this year's Associates—they represent the future of medicine in the United States.

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Outcome of Hepatitis C Patients Treated with Pegylated Interferon and Ribavirin at Roger Williams Medical Center

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Purpose: This study retrospectively evaluated the outcome of a diverse population of Hepatitis C patients treated with pegylated interferon and ribavirin and compared actual real-life results to published clinical trials.

Materials and Methods: The medical records of a total of sixty seven Hepatitis C patients, treated by pegylated interferon and ribavirin, were retrospectively reviewed regarding their outcomes following treatment. The outcome variables considered in our analysis were: sustained virologic response (SVR), breakthrough, relapse, and no response. The different outcomes were plotted against the following variables: patients' age, ethnicity, gender, Body Mass Index (BMI), hepatitis C genotype, Human Immunodeficiency Virus (HIV) status and stage. We also reviewed the treatment-related side effects and compliance to treatment. Results: SVR was achieved in forty one out of sixty seven patients (61.1%). The majority of the patients were in the fifth to sixth decade from whom nineteen out of twenty eight (67.8%) achieved SVR; three out of five patients (60%) were non-white; females had better SVR compared to males (75% versus 54.5%); seventeen out of thirty six patients (47.2%) had genotype 1, thirteen out of fourteen (92.8%) genotype 2, nine out of thirteen (69.2%) genotype 3, and two out of four (50%) genotype 4; one patient had S0 and achieved SVR, four out of twelve (33.3%)S1, eleven out of sixteen (68.7%) S2, eight out of thirteen (61.5%) S3, one out of seven (14.2%) S4 and sixteen out of eighteen (88.8%) had no biopsy. The patients who had no biopsy were mainly genotype 2 and 3; we did not notice a difference in the SVR according to the patients' BMI. Ten out of sixty seven patients (14.9%) had relapse, two out of sixty seven (2.9%) had breakthrough, nine out of sixty seven (13.4%) did not respond, and twelve out of sixty seven (17.9%) did not complete the treatment. All patients developed side effects during their treatment, mainly fatigue (77.6%), flu like illness (32.8%), depression (26.3%) and insomnia (23.8%). Three patients out of the sixty seven (4.4%) developed serious side effects (pancytopenia, myocardial infarction, and suicidal attempt). Conclusion: Patients who have genotype 2 had better SVR compared to patients who have genotype 1. These results match with the statistical results shown in published clinical trials. BMI has no effect on SVR. The majority of nonresponders had genotype 1.

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Effectiveness of Pulsed Electromagnetic Field Therapy on Reducing Proteinuria

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As a major global health concern, proteinuria has been established as an important independent risk factor for cardiovascular disease and renal parenchymal damage leading to end-stage kidney failure. We investigated the efficacy of pulsed electromagnetic field (PEMF) therapy in reducing urinary protein excretion over a 2 week period in subjects with overt nephropathy while continuing optimal mechanisms to reduce proteinuria by inhibition of the renin-angiotensin system (RAS) using supramaximal doses of angiotensin receptor blockading (ARB) agents. Electrotherapeutic technologies has been demonstrated to modulate the calcium calmodulin-dependent, cGMP induced nitric oxide signaling pathway which may con-

fer anti-proteinuric and anti-fibrotic properties by working at the cellular level promoting nitric oxide release, creating a cascade of events including blood vessel dilation, growth factor secretion, angiogenesis and ultimately tissue remodeling.

As a result of activated changes in nitric oxide and intracellular mechanisms following ARB agents, we investigated whether there was a further reduction in proteinuria in subjects on ARB agents when administered PEMF therapy.

Methods: Four well controlled hypertensive volunteers with chronic macroalbuminuria applied low frequency PEMF therapy three times a day for 14 consecutive days, while continuing previously prescribed antihypertensive and RAS inhibitor medications.

No changes were made to drug regimens during the 28-day observation. Proteinuria was expressed as the ratio of protein to creatinine, as determined on adequate twenty-four hour urine collections at baseline, 14 and 28 days after initiation of therapy. Office blood pressure measurements along with serum creatinine, potassium and urea nitrogen concentrations collected at one central location were monitored at 7 day intervals from baseline to study endpoint. The glomerular filtration rate was estimated by means of the Modified Diet of Renal Disease (MDRD) formula. Collected data was analyzed with the use of paired Student's t-test.

Results: After 14 days of PEMF therapy, all participants demonstrated an arithmetic but not statistically significant decrease in urinary protein excretion. Mean urinary protein excretion was reduced by 36%, from 2.85 g of protein per gram of creatinine to 1.80 g of protein per gram of creatinine during the 2 week intervention period PEMF therapy was applied (p = 0.06). Proteinuria gradually increased again over time after discontinuation of PEMF therapy on day 15, resulting in a level of proteinuria that did not differ significantly from that at baseline. There were no significant changes in mean arterial pressures and serum creatinine concentrations during the 28 day observation. No adverse events were reported.

Conclusion: In this primary analysis, our observations demonstrate that additional and synergistic reductions in proteinuria were achieved with PEMF application in patients already receiving optimal pharmacological management to reduce proteinuria by RAS inhibition. Several limitations need to be taken into account such as small sample size and lack of long term follow-up. A larger study is currently in progress evaluating for persistent reductions in proteinuria, as well as the potential effect on possible preservation of renal function.

While the emphasis of our laboratory as well as other researchers have focused on reducing proteinuria through pharmacological means, the advent of electromagnetic fields may confer a new modality which may act synergistically with RAS antagonists to maximally reduce urinary protein excretion in patients already receiving optimal drug therapy and with limited treatment options.

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High Prevalence of Bone Demineralization and Vitamin D Insufficiency in a Cohort of HIV-infected Postmenopausal Women

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In the era of HAART, HIV-infected women will live longer and experience changes related to menopause. Osteopenia is prevalent in persons with HIV and is part of a normal sequence of aging in women. However, there are very little data on bone metabolism in HIV-infected postmenopausal women.

HIV-infected women age > 45 were referred to the HIV Menopause Clinic at the Miriam Hospital (Providence, RI). A woman was considered postmenopausal if she was status-post bilateral salpingo-oophorectomy with or without hysterectomy, or if she had no menses for more than 1 year with elevated FSH and/or LH. Bone mineral density (BMD) was assessed by dual-energy X-ray absorptimetry (DEXA) in the lumbar spine and hip. We then calculated 10-year fracture risk for postmenopausal women with osteopenia using the FRAX tool, which was developed by WHO based on models that integrate the risks associated with clinical risk factors and BMD at the femoral neck.

Thirty-five postmenopausal women were included. Median age was 52 years (range 38-72); 40% Caucasian, 34% African-American, 26% Latino. Median weight was 151 lb (range 99-261). Median follow-up since HIV diagnosis was 14 years. Median CD4 count was 373 cells/L (range 72-1260). 86% were on NRTI-based HAART: 40% with TDF, 28% with NNRTI, and 43% with PI. 63% of subjects had plasma viral loads (PVL) <75 copies/mL. 40% were current tobacco-smokers. 14% were on methadone maintenance. 17% had history of alcohol abuse. 40% self-reported their physical activity being inadequate. 54% did not consume sufficient amount of calcium. Mean serum level of calcium was 9.3 mg/dL and 25-OH Vitamin D was 25.8 ng/ml. 54% were vitamin D deficient (25-OH vitamin D level < 30 ng/mL). Based on WHO criteria, 18% were diagnosed with osteoporosis (t-score <-2.5 SD below normal) and 59% were osteopenic (t-score -1.0 to -2.5 SD below normal). Using FRAX, we found the average 10-year risk for major osteoporotic fracture was 7% and that for hip fracture was 1% for women with osteopenia. No patients in this cohort had a fracture since being infected with HIV.

This cohort-based cross-sectional survey of relatively young HIV-infected postmenopausal women showed a high prevalence of osteoporosis as well as Vitamin D deficiency. As this population ages, the clinical consequences (e.g. fractures) of bone demineralization and Vitamin D deficiency will become apparent. Studies are needed to investigate potential mechanisms and treatment options.

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Medical Residents Behind Bars: A Unique Clinical Experience and Linkage Project

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Prisoners have a high burden of chronic medical conditions. While incarcerated, prisoners are entitled to medical care, but often experience a discontinuity of primary medical services upon release. This leads to poor health outcomes, including an increased risk of death.

Background: In July 2008 a partnership was formed between the medical division of the Rhode Island Department of Corrections (RIDOC) and the Internal Medicine residency program of the Alpert School of Medicine of Brown University with the intention of exposing residents to correctional health, and promoting medical continuity for adult prisoners upon release into the community. In the men's division of the Adult Correctional Institute (ACI), clinic sessions were developed to target inmates with chronic medical problems who were at risk of discontinuity of care upon release. Residents were precepted by RIDOC Board Certified internists at clinics sessions one half day a week and provided medical services to soon-to-be-released inmates. Those without identified plans for community medical follow up were seen by a social worker and referred to the medical residents' clinics at Rhode Island Hospital (RIH) and The Miriam Hospital (TMH) upon release.

Methods: We conducted a review of all inmates seen at the medical residents' clinic sessions held at the minimum security prison during Jan 1-Dec. 31, 2009. Baseline data were self-reported at initial pre-release visits. Patients were then searched against the data repository of RIH / TMH to identify clinical encounters occurring during the period following release. The RIDOC database was also searched for any activity of re-incarceration during the patients' post-release period. Descriptive statistics were generated for demographic and clinical data.

Results: A total of 146 patients were seen over the period. The mean age was 44 years. The most prevalent conditions were hepatitis C (21.2%), injection drug use (19.9%), depression (14.4%) and hypertension (13.0%). Patients were seen at a mean of 35 days prior to release from prison; 76% were referred to residents' medical clinic. A search of the RIH / TMH / RIDOC databases during the post-release period found 29 (19.9%) patients had outpatient medical encounters at a mean of 38 days after release, 26 (18%) had Emergency Department (ED) encounters at 69.5 days, and 41 (26%) had re-encounters with the ACI at 87 days.

Conclusions: Early data suggest our patients are less likely to encounter the ED within 60 days of release than in the general population of released prisoners. Our project represents a novel collaboration incorporating correctional health with medical residents' ambulatory experience and may serve as model of transitional care for adults released from prison. Further studies are needed to better understand the impact of this program on the health outcomes and resource utilization of its patients.

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Characteristics of Adults Hospitalized with Novel 2009 influenza A (H1N1) in a Community Hospital

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Background: Results from studies of the novel 2009 H1N1 influenza early on during the pandemic suggest that the majority of symptomatic patients are young, and clinical disease is mostly mild. Data on patients hospitalized with H1N1 disease in community hospitals are scarce.

Objective: To describe the epidemiological and clinical characteristics of adult patients hospitalized with pandemic influenza A (H1N1) during the peak of the pandemic in a community hospital.

Methods: Review of medical records from adults admitted with laboratory-confirmed novel 2009 influenza A (H1N1) between October 31 and December 9, 2009 at Memorial Hospital of Rhode Island – a teaching community hospital.

Results: A total of 23 (70%) of the laboratory-confirmed adult patients admitted with pandemic influenza H1N1 during this time period consented to study enrollment. Among these, 74% were women, and 26% were men. The median age was 54 (range 22 – 81), and the mean Charlson comorbidity index was 3.7. The majority (91%) of these patients had underlying chronic lung disease, and 57% of the patients were obese (BMI = 30). The diagnosis of novel H1N1 influenza was confirmed by a positive RT-PCR in all cases. The sensitivity of our rapid nucleoprotein antigen test for detecting pandemic H1N1 influenza was only 32%. The median duration of clinical symptoms was 9 days (range 3-22 days), and the median length of hospital stay was 7 days (range 2-19 days). Patients whose symptoms lasted = 10 days were more likely to have a prolonged hospitalization (P = 0.02), and tended to be = age 65 (P = 0.07). Radiological pulmonary infiltrates were present in 61% of the patients. These patients were more likely to have multiple underlying comorbidities (Charlson index = 5, P = 0.06) and hospital stays = 7 days (P = 0.02). The median duration between onset of clinical symptoms and laboratory confirmation of pandemic H1N1 influenza was 6 days (range 2-20 days).

Conclusion: Our preliminary findings suggest that during the peak of the 2009 pandemic, novel H1N1 influenza was associated with significant morbidity in the hospitalized elderly and adult patients with underlying comorbid illnesses. Interestingly, in some hospitalized patients, nasopharyngeal viral samples were positive for influenza by RT-PCR for 6 or more days from clinical onset. Further research addressing risk factors associated with prolonged H1N1 viral shedding would have important infection control implications.

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Oseltamivir Resistant 2009-2010 Pandemic Influenza A (H1N1) in an Immunocompromised Patient

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Although neuraminidase inhibitors are active against most 2009-2010 pandemic influenza A (H1N1) swine-origin strains, since April of 2009, 54 total cases of oseltamivir-resistant H1N1 swine-origin have been reported in the US (as of February 1st, 2010). We report a patient with an underlying hematologic malignancy who was hospitalized with influenza A (H1N1) swine-origin and whose strain developed oseltamivir resistance during therapy.

Case Report: A 26 year-old woman with ALL was admitted to our hospital on November 18, 2009 for re-induction chemotherapy. On admission, her absolute neutrophil count (ANC) was 800 cells/μL. On hospital day 3, she developed a non-productive cough and had a temperature of 102.6 °F with an ANC of 300 cells/μL. She was started on antibiotics and oseltamivir 75mg twice daily. A nasopharngyeal swab sent for a respiratory viral panel revealing probable influenza A (H1N1) swine-origin and rhinovirus. She continued to have fever so antifungal coverage was added, antibiotics were changed, and oseltamivir was continued. Fevers persisted, and bronchoscopy was performed. Viral culture derived from the bronchoscopy specimen grew influenza A (H1N1) swine-origin. The patient continued to have daily fever in the setting of prolonged neutropenia. On hospital day 17, a nasopharyngeal swab again revealed H1N1, as well as rhinovirus, despite 13 days of oseltamivir, and the concern for resistance was raised. Antiviral coverage was changed to zanamivir, and a nasopharyngeal swab culture was sent for resistance testing. A nasopharyngeal swab was used for respiratory viral panel testing on day 20 which was negative. On day 23, viral cultures from a nasopharyngeal swab done on day 17 returned positive for oseltamivir-resistant influenza A with the H275Y mutation. Despite aggressive therapy, she died on hospital day 40. After her death, we performed resistance testing on a stored sample of the initial influenza strain isolated on hospital day 3; it was sensitive to oseltamivir. Additional testing was also performed on the bronchoscopy specimen from hospital day 11, which demonstrated that resistance to oseltamivir had developed after eight days of oseltamivir therapy.

Discussion: To our knowledge, this is the first case of oseltamivir-resistant, swine-origin influenza A (H1N1) that was associated with death. In the United States, 42 of 54 individuals with resistance had documented exposure to oseltamivir, suggesting that resistance develops under selective pressure to the drug and not as a natural variant. We have shown that resistance developed during oseltamivir treatment in our patient who was receiving the recommended dosing of 75mg twice a day. Recent literature suggests that an increased dose of 150mg twice a day may be preferable for critically ill patients. Oseltamivir resistance should be a consideration when treating critically ill or immunocompromised patients.

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