

Abstracts: Rhode Island Chapter, American College of Physicians 2008 Annual Meeting Associates Forum Competition Winners

The Rhode Island Chapter of the American College of Physicians in April of 2008 hosted its Annual Associates Forum Competition and Podium Presentation. There were over seventy submissions from Residents in the four teaching programs at Rhode Island hospitals. A committee of program directors made the difficult choice of picking seven winners.

At the Annual meeting we had a distinguished panel of three judges as well as over 100 attendees listen to the presentations. There were a mixture of Clinical Vignettes with a literature review and Original Research. All the presenters had outstanding projects, with topics ranging from a “Fever of Unknown

Origin” to the “Quality of Sleep in Hospitalized Patients”.

The seven podium presenters each received a plaque and a cash reward from the College Chapter. It is reassuring and inspirational to know that these outstanding Associates are the future of medicine in the United States. Congratulations to all the participants in this year’s competition.

– N.S. Damle, MD, FACP
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Fever of Unknown Origin

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DC, a 41 year-old man with a history significant for adult onset diabetes mellitus and recent immigration from Brazil, presented to the hospital with daily fevers for 5 weeks. He also complained of vague diffuse abdominal pain associated with nausea, history of watery diarrhea (now resolved) weight loss. The patient had traveled from Brazil through the Americas to Rhode Island, living outdoors and drinking brackish water. Several members of his traveling party fell ill with similar symptoms. He did not recall any rashes or insect bites during his travels.

Physical exam on admission revealed temperature of 103.2 degrees Fahrenheit and vital signs otherwise within normal limits. Abdominal exam revealed diffuse tenderness, slightly worse in the right upper quadrant and mild splenomegaly. No lymphadenopathy or skin changes were noted and physical exam was otherwise unrevealing.

Labs upon admission were notable for pancytopenia (WBC 1600 with 71% segmented cells and 4% bands, hemoglobin 9.7 g/dL and platelets 67,000). Mild hemolysis was noted with 1+ schistocytes on peripheral blood smear, reticulocyte count 5%, LDH 552 IU/L, Haptoglobin 17 mg/dL. Liver function tests showed elevated AST 127 IU/L, ALT 242 IU/L, Alkaline Phosphatase 263 IU/L and hypoalbumenia 2.5 g/dL. Ferritin was elevated at 11,711 ng/mL. A CAT scan of the abdomen revealed only mild splenomegaly. Blood and urine cultures were negative. An extensive work up for fever of unknown origin followed. Ehrlichia, and Babesia titres, HIV ELISA and viral load, parasite smears x 3, and hepatitis serologies were all negative. EBV and CMV titres were IgG positive only. PPD was placed and did not react. Empiric treatment with Ceftriaxone for possible typhoid fever was started without good clinical result. A continuing FUO work up was pursued. FTA-ABS was positive but RPR was negative. Stool studies were all negative. Brucella, tularemia, histoplasma, coccidoides, Q fever, blastomycoses, leptospira, strongyloides and bartonella serologies were all negative. Typhoid, dengue, parvovirus, schistosomiasis serologies all showed evidence of prior exposure

but not acute infection. During his hospital stay, a new genital ulcerating lesion was noted. HSV DFA was positive upon swab of this lesion and the patient was placed on Valcyclovir for treatment.

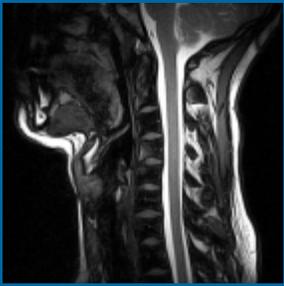
The patient underwent bone marrow biopsy, which revealed poorly formed granulomas but negative cultures and AFB. Liver biopsy was done, which also showed microgranulomas. On hospital day 26, despite no organisms being identified on liver or bone marrow biopsy, Leishmaniasis titres were sent. His Leishmaniasis titres returned as IgG + for L Donovanii and L. Braziliensis. The CDC was contacted and his original liver biopsy sample was sent to the Armed Forces Institute of Pathology. Further review there by an expert in the disease identified the intracellular amastigotes consistent with leishmaniasis. On hospital day 42, he was started on liposomal amphotericin for treatment of leishmaniasis. After 3 days of therapy, he defervesced. His labs did not improve, but he was discharged home in stable condition on hospital day 48 with outpatient infusion of day 14 and day 21 liposomal amphotericin.

Discussion: There are an estimated 500,000 new cases of symptomatic **visceral leishmaniasis (VL)** a.k.a kala-azar yearly; 90% of cases are reported from endemic regions of Bangladesh, India, Sudan and Brazil. Visceral disease is most often caused by the species of the *L. donovani* complex, for which our patient had IgG positivity. Leishmaniasis parasites are carried by the sandfly vector. Clinical disease occurs on a spectrum with marked immune response causing mucocutaneous leishmaniasis at one end and lack of granulomatous inflammation (ie visceral leishmaniasis and diffuse cutaneous leishmaniasis) at the other end. Five classic features make up VL disease: organomegaly, fever, cachexia, pancytopenia and hypergammaglobulinemia. Darkening of the skin also occurs commonly in India with VL. These features in a patient living in an endemic area should highly suggest the diagnosis. Diagnosis is confirmed by visualizing amastigotes in tissue or promastigotes in culture. Splenic aspiration is the most sensitive, followed by bone marrow aspiration. Lymph node and liver biopsy can also be used. Antileishmanial antibodies are often positive in high titers in im-



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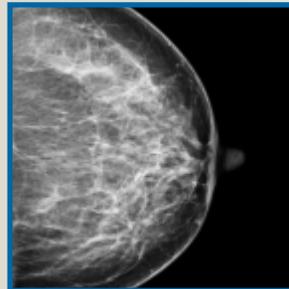
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munocompetent patients with VL. In summary, visceral leishmaniasis should be on the differential for fever of unknown origin in patients traveling to or from endemic areas.

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Hypokalemic Thyrotoxic Periodic Paralysis in a Young African American Male

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A 26-year-old African American gentleman presented with a one-day history of profound upper and lower extremity weakness and a one-week history of watery diarrhea. For two days prior to admission, when the patient awoke he noted extreme difficulty moving. The symptoms would gradually resolve and he would be able to carry out his daily activities. However, on the day of admission he awoke with weakness so profound that he could not stand up. He then became anxious and noted SOB, nausea, and diaphoresis, at which point he called rescue and was brought to the hospital. ROS were notable for several months of DOE, frequent palpitations, and insomnia. The patient denied using any medications or illicit substances. Initial examination was remarkable for tachycardia, thyromegaly, and 3+ reflexes. Laboratory results demonstrated hypokalemia (1.3) and hypophosphatemia (<1.0). Thyroid function studies revealed hyperthyroidism (TSH: <0.03, FT4 : 4.09, T3: 447).

The patient's EKG showed atrial fibrillation with LAD. He was admitted to the ICU, where his potassium was repleted and he was started on PTU and propranolol. It was felt that his hyperthyroidism was secondary to Graves Disease. He clinically improved initially; however, his course was complicated by SOB on HD #2. A CT Angiogram demonstrated mediastinal LAD and bilateral infiltrates, which were thought to be secondary to his thyroid disease and atrial fibrillation, respectively. After complete electrolyte repletion he no longer noted any weakness. He returned to sinus

rhythm and his SOB resolved. He was discharged on PTU and propranolol and was scheduled for endocrinology follow-up.

Discussion: **Thyrotoxic Periodic Paralysis (TPP)** is a rare neuromuscular disorder characterized by concomitant thyrotoxicosis, paralysis, and hypokalemia. It typically affects Asian men between the ages of 30-50, although it can occur in other ethnic groups. The pathophysiology of TPP is believed to be from increased Na⁺ - K⁺ - ATPase muscle ion channel activity in the setting of thyrotoxicosis. This results in increased cellular uptake of potassium, which can further be exacerbated by a high insulin state, causing paralysis in genetically predisposed persons. TPP clinically presents as weakness or flaccid paralysis occurring either a few hours following vigorous exercise, or early in the morning after a high-carbohydrate meal. The degree of muscular involvement and the severity of the attacks can vary widely, although characteristically there is greater proximal muscle involvement. The diagnosis is based on the absence of family history, and the presence of biochemical thyrotoxicosis and hypokalemia. Treatment consists of potassium supplementation, b-blockade, and anti-thyroid medications.

Although TPP usually has a benign course, early diagnosis and restoration of the euthyroid state is essential to prevent recurrent, potentially life-threatening, episodes of paralysis.

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Predicting HIV Viral Load by Immunological Trends: Implications for Identification of Treatment Failure in Resource-poor Settings

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Treatment failure during highly activated anti-retroviral therapy (HAART) is best defined as a persistent detectable HIV plasma viral load (PVL). In resource-poor settings, laboratory assays for PVL are often unavailable due to financial and infrastructure constraints. The paucity of available second-line antiretroviral drugs makes deciding when to change HAART a challenge. Recognizing these limitations, the World Health Organization published HIV treatment guidelines in 2006 and defined treatment failure based on immunological criteria as: 1) A decrease of CD4 cell count to pre-therapy baseline levels or below; 2) A 50% decrease from the on-treatment peak value; and/or 3) Persistent CD4 count levels below 100 cells/mm³. Clinical practice in many resource-poor settings rely on at least a greater than 25% decrease in CD4 cell count to define treatment failure during HAART. Current literature suggests that CD4 counts are not strongly associated with PVL and that CD4 percent may be a more accurate predictor of PVL. To further define the relationship between CD4 cell count, CD4 percent, and PVL, we obtained data on 303 pa-

tients from the outpatient HIV clinic at The Miriam Hospital. Patients were eligible if they were on HAART for at least six-months, and had CD4 and PVL data available during this time. We examined proportions of virologic failure based on immunological trends using the Chi Square and Fisher Exact tests. A > 10% decline in CD4 percent over a six month time period was significantly more likely to predict a detectable PVL when compared to any decrease in absolute CD4 cell count (18/41 patients with a CD4 percent decrease > 10% had an undetectable PVL, versus 71/102 for any decrease in CD4; p=0.007). On the other hand, a > 25% decline in absolute CD4 cell count was not able to predict a detectable PVL better than using any decrease in CD4 percent (p>0.10). A > 50% decrease in absolute CD4 cell count was only significantly better at predicting a detectable PVL for a decreasing CD4 cell percent less than 5% (p=0.04). A persistent CD4 level below 100 cells/mm³ compared to a persistent CD4 percent below 7% was not able to better predict a detectable PVL (p=0.62). We conclude that decreases in CD4 percent may be a more accurate pre-

dictor of a detectable PVL and thus of treatment failure. The incorporation of CD4 percent trends as a secondary marker to guide treatment decisions may be helpful in resource poor settings.

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Methicillin-Resistant Staphylococcus Aureus Colonization of Surgical and Medical Residents

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In healthcare settings, transmission of **Methicillin-Resistant Staphylococcus aureus (MRSA)** to patients is most often from **healthcare workers (HCWs)** who have less than optimum hand hygiene. According to CDC guidelines, surveillance cultures for MRSA are not routinely recommended for HCWs unless epidemiologically linked to clusters of cases among patients. Rates of MRSA colonization of HCWs are generally unknown, particularly among house staff. Similarly, it is unknown if differences exist in MRSA colonization among medical and surgical house officers as a result of differences in exposure, procedures done, etc. The purpose of our study was to determine the prevalence of MRSA carriage in medical and surgical house staff. Our null hypothesis was that there was no difference between the two groups of house officers.

METHODS: During a one-month period, fifty medical and fifty surgical residents at Rhode Island Hospital were enrolled in a prospective, point-prevalence survey of MRSA nasal carriage. In addition to obtaining nares cultures for MRSA, each resident completed a brief questionnaire about their perceptions of hand hygiene and isolation precautions used when examining patients with

MRSA. This investigation was approved by the hospital IRB. A 2-tailed Fischer exact test was used for statistical analysis.

RESULTS: Five surgery residents (10%) and zero medical residents were found to have a positive nares culture for MRSA ($p=0.03$). Of the surgery residents who were MRSA-positive, 3 of 22, 2 of 9, and 0 of 19 were PGY1, PGY2, and PGY3-10, respectively ($p=0.1$ for MRSA carriage among PGY1 and 2 vs. PGY3-10). **CONCLUSION:** There is a higher prevalence of MRSA in the nares of surgical vs. medical house staff. The reason for this difference is not known, but may be related to greater direct contact with MRSA-infected wounds among surgical residents vs. medical residents. There may be a higher risk of MRSA carriage among surgical residents earlier in their training when they have a more direct role in post-operative wound care. Further research is necessary to help fill gaps in our knowledge of colonization in house staff.

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Genetic and Functional Adaptation of Pancreatic Beta Islets To Pregnancy: Potential for Gene Therapy In Diabetic Patients

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In vitro studies have demonstrated that pregnancy-influenced murine pancreatic beta cells are capable of secreting more insulin during pregnancy than non pregnant controls. Also it has been observed that murine pancreatic beta cells undergo active proliferation during the last week of pregnancy and return to a quiescent status two days post delivery (pd2).

To the best of our knowledge there have been no studies to evaluate the function of pancreatic islets from pregnant mice after transplantation into non pregnant mice.

AIMS: To prove that islets, under the influence of a gestational environment, exhibit improved functionality, even when ectopically transplanted into non pregnant mice, and to determine the genetic profile in pancreatic islet during pregnancy.

METHODS: Diabetes was chemically induced in female mice recipients and was defined by blood sugar (BS) 300 mg/dl. Islets were isolated from syngeneic pregnant day 7, day 15, pd2, and non pregnant female donors. Recipient mouse received islet transplantation under one kidney capsule. Recipient mice were divided into three groups. The first group received full mass transplantation of 600 islet equivalent (IEq), the second received suboptimal mass of 400 IEq, and the third group received marginal mass of 200 IEq. Blood sugar was checked three times a week. Reversal of diabetes was defined as

BS less than 200 mg/dl. Grafts were later harvested and analyzed. Gene profile was performed after islets were isolated from pregnant mice on days 7, 14, 15, 18, pd2 and control non pregnant mice.

RESULTS: Reversal of diabetes was observed in 75% of marginal mass recipients from pregnancy day 15 donors, and 100 % in marginal mass recipients from pd2, but there was no reversal in recipient from day 7 and control none pregnant donors. The statistically significant and two fold differentials in genetic venations were as follow: Control versus day 7 and day 14: no difference. Control versus day 15: 34 genes Control versus day 18: 54 genes Control versus pd2: 23 genes Some of these genes are related to proliferation, migration, secretion, or apoptosis.

CONCLUSION: Pancreatic islets isolated from animals on their last third of pregnancy (P15 and pd2) demonstrate improved functionality and reverse diabetes, preserving long-term euglycemia, in a marginal mass transplant model. We have identified a number of genes the expression of which is significantly changed during pregnancy in association with islet proliferation that could be a potential for gene therapy in diabetic patients.

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Effects of Erythropoietin Adjust Automated Protocols on Hemoglobin Levels in ESRD Patients

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Background: Recent anemia studies have demonstrated increased mortality in patients with hemoglobin (Hb) levels >13g%. As a result, the FDA instituted a Black Box Warning "to use the lowest dose of erythropoietin stimulating agents (ESAs) that will gradually increase the hemoglobin concentration to the lowest level sufficient to avoid the need for red blood cell transfusion." In addition, other recent clinical trials have shown adverse outcomes with Hb <11g%. We evaluated Hb variability following alterations in erythropoietin adjust protocols with goals to reduce subjects with Hb >13g%. Changes in Hb <11g% and >13g%, and related variables, were analyzed to determine effects of ESA dose on hemoglobin. **Methods:** We designed a retrospective cohort study in 7021 patients treated in 120 dialysis facilities at DSI Renal, Inc. from January-December, 2007. We investigated variability in serum Hb levels, for Hb <11g% and Hb >13g%, and other variables (Ferritin-Reticulocytes-URR-Iron Saturation). Comparisons were made among three groups; the original erythropoietin anemia protocol-A (Jan-April (pre-FDA)), protocol-B (May-Aug (post-FDA)) and protocol-C (Sep-Dec (modified to optimize Hb target 11-12g%)). The intent of protocol-B was to reduce the % of dialysis patients with Hb >13g%. After demonstrating a main effect by ANOVA, Student's t-test was performed utilizing Bonferroni correction factor.

Results: In subjects with Hb <11g%, ANOVA showed $p=0.0045$ for protocol periods A, B and C. Student's t-test between protocols A-B ($p=0.0005$), and B-C ($p=0.0226$) were significant. For Hb >13g%, ANOVA was $p=0.0061$ with changes only from A-B ($p=0.004$), although there was an arithmetic increase from B-C ($p=0.054$). Other parameters analyzed showed no significance by ANOVA (Ferritin-Reticulocytes-URR). Although Iron Saturation was significant ($p=0.033$) by ANOVA, Student's t-tests between A-B and B-C were non-significant. Nearly twice as many patients had a significant increase in Hb <11g% compared to a reduction in Hb >13g% during protocol B.

CONCLUSIONS: These data demonstrated a significant increase in subjects with Hb <11g% between A-B and a reduction from B-C, while for Hb >13g%, there was a significant reduction between A-B, and an arithmetic, but non-significant increase during B-C. These changes may be related to delayed erythropoietin effects that may occur over several weeks in response to changes in total ESA dose, or other influences on Hb levels. Further analysis is required to better understand relationships between hemoglobin variability, total erythropoietin dose, the number of months out of the established Hb target and their effect on mortality.

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Quality of Sleep In Hospitalized Patients

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Background: Sleep affects health, daytime function and quality of life. Hence measurement of sleep quality in hospitalized patients is important as it may offer an intervention target to improve clinical outcomes. A basic assessment of sleep quality can be done with sleep diary, sleep log and sleep questionnaire. Insomnia is a subjective complaint of dissatisfaction with the quantity, quality or timing of sleep. Insomnia affects approximately 12 to 25% of the general population and is more prevalent in hospitalized patients. In hospitalized patients, the most common causes of acute insomnia includes the effects of illness, environmental sleep disruption, medication, anxiety and depression. We conducted a questionnaire study to understand quality of sleep and factors affecting sleep in hospitalized patients.

Methods: This single-centre prospective study involved an assessment of sleep quality for consenting patients admitted to the general medical floor at RWMC. Each patient was given questionnaires asking them about their quality of sleep, use of sleep aids, factors disrupting sleep as related to the illness or hospital environment. They completed a sleep diary and a daily questionnaire during hospital stay. A final discharge day questionnaire was completed summarizing their sleep during hospital admission. Each patient was asked to make any additional comments about their sleep.

Results: 35 patients were enrolled at random (19 males, 16 females) who suffered from multiple chronic diseases. The TST at home was $8.8 + 1.6$ hours versus $9.4 + 1.1$ hours in hospital ($p=0.04$). Nocturnal awakenings were increased during hospital stay ($1.66 + 0.64$) compared to home ($1.02 + 1.25$, $P=.009$). Daytime naps at home were reported by 1% compared to 99% in hospital. The average total daytime nap time was 1 hour at home and 3 hours in hospital. 43% of subjects received some kind of sleeping aid at home compared to 74% in hospital. Patients reported a very high impact of hospital environment on their sleep - 9 on a 0-10 scale. Their illness was also perceived to be impacting quality of sleep - score of 7 on the same scale of 1-10.

Conclusion: Overall patients had more fragmented sleep even though the total sleep time was increased in the hospital. Patients reported a bigger impact of hospital environment (noise, TV, nursing, roommates, blood draws, vital checks etc) than medical illness on sleep quality. More nighttime awakenings led to increase in daytime naps to compensate for the total sleep time. Data regarding differences due to hypnotic administration during hospital stay will also be presented (not yet analyzed).

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