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**Handbook of Abstracts**

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## **Acknowledgment of Mentors**

1. Lindsay Arnold, Pharm D
2. Jessica Bender, MD
3. Emelia Benjamin, MD
4. Sheilah Bernard, MD
5. Jonathan Berz, MD
6. Katherine Bever, MD
7. Anthony Breu, MD
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19. Brian Jacobson, MD
20. Karen Jacobson, MD
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22. Jared Magnani, MD
23. Marie McDonnell, MD
24. James Meisel, MD
25. Edward Miller, MD
26. Paul Monach, MD
27. Eleftherios Mylonakis, MD (Brown University)
28. Mathew Nitzberg, MD
29. David Nunes, MD
30. Michael Paasche-Orlow, MD
31. Nadine Palermo, MD
32. David Pemental, MD
33. Jonathan Pincus, MD
34. Sandhya Rao, MD
35. Flora Sam, MD
36. Vaishali Sanchorawala, MD
37. Mark Sloan, MD
38. Lauren Stern, MD
39. Judith Strymish, MD
40. Minh-Tam Truong, MD
41. Allan Walkey, MD
42. Renda Wiener, MD

## Category: Clinical Research

### Evaluation of Aspirin Use in Patients with Atrial Fibrillation with Stable Coronary Disease requiring Warfarin

Shazia Ahmad<sup>1,2</sup>, Josef Bozzay<sup>1</sup>, Mumtaz Y. Balkhi<sup>3</sup>, Devin O' Hara<sup>1</sup>, Atul Singh<sup>1</sup> and William H. Carter<sup>1</sup>

1 Department of Internal Medicine, West Virginia University, Charleston, WV, USA.

2 Boston University Medical Center, Boston, MA.

3Tufts University Medical Center.

**Background:** Atrial fibrillation is the most common type of arrhythmia and is associated with an increased risk of stroke and heart disease. Most patients with atrial fibrillation need long term anticoagulation to reduce the risk of stroke, however, anticoagulation is associated with an increased risk of bleeding. In February 2012, CHEST guidelines on anti thrombotic therapy for AF reiterated that dual therapy of aspirin with warfarin increases bleeding risk nearly twofold. Therefore, warfarin without aspirin for the first time was recommended in patients with atrial fibrillation and stable coronary artery disease.

**Objective:** In the current study we investigated anticoagulation practices by clinicians for patients with atrial fibrillation and stable coronary artery disease, before and after the recent publication of the 2012 CHEST guidelines. We also examined retrospectively if bleeding risk or stroke risk influenced the physician decision to use aspirin with warfarin.

**Patients and Methods:** We performed a retrospective study on 100 randomly selected patients, eighteen years or older with atrial fibrillation and stable coronary artery disease, hospitalized between January 1, 2011 through March 1, 2012 (pre-CHEST Guidelines) and March 1, 2012 through July 31, 2012 (post-CHEST Guidelines). Bleeding Risk Score and CHADS-2 scores were calculated. Statistical significance was calculated through Fischer Exact test.

**Results:** No change in practice by clinicians following 2012 CHEST Guidelines was observed. Aspirin use was documented in only in 50-60% of patients with stable coronary artery disease both on admit and discharge. No significant difference was observed in prescription of antiplatelet

## Category: Clinical Research

### Utility of FDG-PET in Determining the Response to Immunosuppression Treatment in Cardiac Sarcoidosis

Ahmadian A; Ruberg FR; Berman JS; Govender P; Miller EJ

**Background:** Immunosuppressive treatment to reduce cardiac inflammation is commonly employed for patients with cardiac sarcoidosis (CS) despite a lack of objective data to support its use. FDG-PET can be used to measure inflammation in CS, potentially making this imaging technique a useful way to follow immunosuppression, but interpretive methods for FDG-PET imaging are not standardized. New quantitative methods of interpreting FDG-PET may provide a more accurate measurement of changes in cardiac inflammation in CS, but data comparing interpretive methods has not been described. We investigated the response to treatment of various qualitative and quantitative measures of cardiac FDG uptake on FDG-PET, as well as if FDG uptake recurred after cessation of immunosuppressive treatment.

**Methods:** FDG uptake on serial FDG PET/CT studies (39 studies/15 patients) before/after immunosuppression in patients with CS was determined by qualitative (FDG(+) segments, visual interpretation) and quantitative (cardiac SUVmax, volume of FDG(+) myocardium using multiple thresholds, volume-intensity) methods.

**Results:** In 93% of patients (14/15), prednisone-based immunosuppression (mean dose  $36.5 \pm 33.4$  mg, mean duration  $276 \pm 112$  days) lead to a reduction in FDG volume, with complete response (zero measurable FDG uptake) in 9/15 patients. Visual FDG uptake changed in only 7/14 patients. In 6 patients with scans performed for surveillance after the cessation of immunosuppression ( $110 \pm 159$  days post-treatment), 3/6 had a rebound increase in FDG volume but no patient returned to maximum/pre-treatment FDG uptake.

**Conclusions:** Interpretation of FDG-PET in CS using volumetric measures of FDG uptake a sensitive method for evaluating response to immunosuppression, suggesting quantitative FDG PET techniques may be superior for following serial FDG-PET studies in CS. Cessation of treatment leads to a mild rebound increase in FDG uptake compared to treatment. Further studies are needed to see if reduction and/or resolution of FDG uptake in CS are associated with improved clinical outcomes.

## Category: Clinical Research

### Clinical Presentation and Treatment Responses In IgM-Related AL Amyloidosis

Moussa Sissoko MD; Vaishali Sanchorawala MD; David Seldin MD, PhD; Brian Sworder MD; Kenneth Angelino MD; Mike Broce BA; John Berk MD; J Mark Sloan MD.

**Objective:** AL amyloidosis is a multiorgan disease due to deposition of misfolded monoclonal immunoglobulin light chains. AL amyloidosis with IgM paraproteinemia is a rare variant of this disease; accounting for approximately 6% of AL amyloidosis cases. The clonal cell of origin may be a plasma cell or lymphoplasmacytic cell, and treatments targeting each have been employed. This study describes clinical and laboratory features of IgM AL amyloidosis patients and their response to different therapeutic regimens.

**Methods:** 106 patients with IgM-related AL amyloidosis were evaluated at the BUMC Amyloidosis Center during 1996-2012. Of the 93 patients, treatment and response information was available on 46 treated after 2003, during the era of new agents for plasma cell diseases. In this cohort, there were 5 treatment groups: high-dose melphalan/stem cell transplant (HDM/SCT); bortezomib-based regimens; standard doses of the alkylating agents melphalan or cyclophosphamide; immunomodulatory agents (IMiDs); and rituximab-based regimens. Treatment regimens were assigned by bone marrow pathology and patient-specific factors.

**Results:** For the 106 patients, the median age at diagnosis was 67 years (range: 38-89 years) with 52 (56%) males. The kidney was the most commonly involved organ (51%) followed by heart (41%) and GI tract (23%). Median IgM was 590 g/dL (range: 29-9130). The clonal population had lambda light chain restriction in 69% of patients. For the 46 patients treated after 2003, overall response rates and rates of very good partial or complete responses were 100% and 80% respectively, with HDM/SCT; 82% and 30% with bortezomib-containing regimens; 80% and 25% with regimens that included rituximab; 75% and 0% with regimens in which an IMiD was included; and 63% and 20% with other alkylator regimens. There was no association between treatment response and organ involvement, sex, or age.

**Conclusions:** Patients with IgM associated AL amyloidosis requiring treatment have a favorable overall survival compared with other forms of AL amyloidosis. Lymphoplasmacytic infiltrates were identified in fewer cases than expected from the series of patients with IgM monoclonal gammopathy of undetermined significance, perhaps because small populations of these cells are not identified by our standard approach. A variety of effective treatment options exist for IgM associated amyloidosis, but testing patients for specific mutations may be a more effective way of assigning diagnoses and targeting therapies (i.e. rituximab or ibrutinib). This study was limited by small sample sizes.



## Category: Clinical Research

### Associations of Adiposity and Atrial Fibrillation in Older Adults: the Health ABC Study.

Konstantinos N. Aronis, MD<sup>1</sup>; Na Wang, MA<sup>2</sup>; Caroline Phillips, MS<sup>3</sup>; Emelia J. Benjamin, MD, ScM<sup>4,5,6</sup>; Gregory M Marcus, MD<sup>7</sup>; Anne B Newman, MD, MPH<sup>8</sup>; Nicolas Rodondi, MD MAS<sup>9</sup>; Suzanne Satterfield, MD, DrPH<sup>10</sup>; Tamara B. Harris, MD, MS<sup>3</sup>; Jared W. Magnani, MD, MSc<sup>4,5</sup>.

<sup>1</sup> Department of Medicine, Boston Medical Center, Boston University, Boston, MA, <sup>2</sup> Data Coordinating Center, Boston University School of Public Health, Boston, MA, <sup>3</sup> Intramural Research Program, National Institute on Aging, National Institutes of Health, University of California, San Francisco, CA, <sup>4</sup> Cardiology Section, Department of Medicine, Boston University School of Medicine, Boston, MA, <sup>5</sup> Framingham Heart Study, Framingham, MA, <sup>6</sup> Department of Epidemiology, Boston University School of Public Health, Boston, MA.

<sup>7</sup> Electrophysiology Section, Division of Cardiology, University of California, San Francisco, CA, <sup>8</sup> Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA,

<sup>9</sup> Department of General Internal Medicine, University of Bern, Switzerland

<sup>10</sup> Department of Preventive Medicine, University of Tennessee Health Science Center, Memphis, TN.

**Introduction:** Obesity is a well-recognized, modifiable risk factor for atrial fibrillation (AF). Limited studies have examined adiposity measures other than body mass index (BMI) and AF risk. We examined associations of adiposity measures with incident AF in a biracial cohort of older adults. Given the extensive racial differences between obesity and AF, we assessed for racial differences in relating adiposity and AF.

**Methods:** The Dynamics of Health, Aging, and Body Composition Study is a prospective cohort of 3,075, community-dwelling, older adults. Adiposity measures were determined using anthropometry [BMI and abdominal circumference (AC)], CT [subcutaneous and visceral fat area (SAT, VAT)] and DXA (total and percent fat mass). AF was identified from the Center for Medicare and Medicaid Services. We determined the associations between adiposity measures and the 10-year risk of incident AF using Cox proportional hazards models. We examined for interactions between race and adiposity measures with the outcome of AF.

**Results:** The cohort consisted of 2,717 participants (mean age 74±3 years, 51.7% women, 41.4% black). The 10-year incidence of AF was 16.6 (95% CI: 14.9-18.3) per 1000 person-years (371 events). In multivariable-adjusted models, every 1-SD increase in BMI, AC and total fat mass was associated with a 13-16% increase in AF risk (HR: 1.14, 95%CI: 1.02-1.28, HR:1.16, 95%CI: 1.04-1.28 and HR: 1.13, 95%CI: 1.002-1.27). Percent fat mass, SAT and VAT area were not associated with incident AF. We did not identify effect modification by race between the adiposity measures and AF risk.

**Conclusion:** We determined that BMI, AC and total fat mass, but not SAT or VAT are associated with 10-year AF risk in a biracial cohort of older adults. As obesity is one of the few modifiable AF risk factors, future studies are required to evaluate how weight change can modify the incidence of AF.

## Category: QI/ Education

### Rapidly Progressive Dementia: Everyone Deserves a Trial of Steroids

Christopher Atkinson, MD

**Introduction:** Rapidly progressive dementia may be caused by prion disease, viral encephalitis, or autoimmune reactions. It is imperative to identify the latter, because it may be treatable.

**Case Description:** A 78 year old man with kidney transplant on immunosuppression and T11 paraplegia due to spinal cord injury presented with acute onset garbled speech and confusion. In the month prior, he had been performing IADLs, however had several episodes of confusion and emotional lability which his family noted were out of character. Physical exam revealed somnolence, incoherent and repetitive speech, unable to follow commands, and myoclonic jerking of both upper extremities. He was initially treated empirically for meningitis and herpes encephalitis, however his condition deteriorated, and he was intubated due to inability to protect airway. CT and MRI showed no evidence of stroke, mass, global atrophy, or basal ganglia changes. EEG showed diffuse slowing, and deep sleep characteristics consistent with encephalopathy. He had no leukocytosis, renal function and electrolytes were at baseline, and tacrolimus levels were not elevated. CSF showed mildly elevated protein with normal WBC, RBC, and glucose and no growth from cultures. He had negative anti-Yo, anti-Hu, and anti-Ri antibodies. VDRL assay, Cryptococci antigen, West Nile antibody, VZV, CMV, JC virus, and Herpes simplex PCR negative. Negative for Tau proteins, and CJD 14-3-3. Anti-TG and anti-TPO antibodies were negative. Patient was hypothesized to have an autoimmune encephalitis due to anti-voltage gated potassium channel antibodies (VGPC), so treatment was initiated with high-dose corticosteroids. He subsequently improved in mental status, and was extubated. Over the next week, he regained executive function and was able to read the newspaper and discuss his medical conditions with good insight. Curiously, VGPC antibody eventually became negative. The patient ultimately passed away from co-morbidities related to end stage renal disease, before further work-up was done. His dramatic response to corticosteroids, however, allowed him to have meaningful interactions with his family during his final weeks.

**Discussion:** This case illustrates the work-up for rapidly progressive dementia. Unlike more common forms of dementia, rapidly progressive dementias can develop over the span of days to months. The differential should include infectious etiologies, toxic metabolic syndromes, paraneoplastic syndromes, auto-immune syndromes, and prion disease. In this case, the patient was initially at a high risk for an infectious or toxic metabolic cause, given his immunosuppression and renal failure, so treating him with steroids for presumed auto-immune encephalopathy had a clinically significant risk. It is curious that his Anti-TG, anti-TPO, and VGPC antibodies were negative. Sometimes in Hashimoto's encephalopathy, Anti-TG, anti-TPO don't become positive until late in the course of illness. Furthermore, there are auto-immune channelopathies other than anti-VGPC antibody syndrome which may respond to corticosteroids.

## Category: Clinical Research

### Outcomes of Patients with a Do-Not-Intubate Code Status who Use Noninvasive Mechanical Ventilation

Lisa Bajpayee, MD<sup>1</sup>; Renda Soylemez Wiener, MD, MPH<sup>1,2</sup>

1 The Pulmonary Center, Boston University School of Medicine, Boston, MA; 2 ENRM VA Hospital, Bedford, MA

**Rationale:** The use of non-invasive ventilation (NIV) can improve outcomes in certain reversible causes of dyspnea. At times it is offered as a final therapeutic option in patients with a do-not-intubate (DNI) code status in lieu of mechanical ventilation or transitioning to comfort care; however, little is known about the epidemiology or outcomes of DNI patients who use NIV.

**Methods:** We conducted a retrospective study at Boston Medical Center—a large, urban, academic teaching hospital—in which we reviewed 120 randomly selected patient charts of patients who were DNI and used NIV to treat their acute respiratory failure between the years 2000-2013. We assessed demographics, etiology of respiratory failure, changes in code status, discharge status, and mortality rates two years after the hospitalization.

**Results:** Among these 120 patients, the average age was 73.4 years, 46% were male, and racial distribution included 60% Caucasian, 31% African American, and 9% other. The etiology of acute respiratory failure included both reversible causes (e.g., chronic obstructive pulmonary disease, congestive heart failure, pneumonia; n=76), and nonreversible causes (e.g., end-stage cancer, neurological disorder, pulmonary hypertension; n=44). During the initial hospitalization, 58 patients (48%) changed their code status from DNI to comfort measures only (CMO), while 14 (12%) reversed their code status to full code and were intubated. Among the 14 who were intubated, 9 (64%) died during the initial hospital stay. More than half of the patients in our cohort (56%) died during the initial hospitalization or were discharged to hospice with the expectation of imminent death. Hospital mortality was higher when NIV was used for non-reversible causes of respiratory failure, as compared to reversible causes (80% vs 23%,  $p=0.0001$ ). Among the 53 patients that survived the hospitalization, 37 (70%) were discharged to a rehabilitation facility and 16 people (30%) were discharged home; however, at least 21 of these patients (40%) were readmitted and died within the next 2 years.

**Conclusions:** Patients who are DNI and receive NIV for treatment of acute respiratory failure have a high overall mortality, with death occurring either in the hospital stay or shortly thereafter. NIV was most successful in treating reversible causes of respiratory failure. This data should be useful when counseling DNI patients and their families on the outcomes of noninvasive mechanical ventilation.

## **Category: Quality Improvement / Education**

### **Early Family Meetings in the ICU for Patients with Metastatic Cancer and Cardiac Arrest: Results from a Quality Improvement Initiative**

Nicholas Bosch,<sup>1</sup> Julian Mesa,<sup>1</sup> Sagar Patel,<sup>1</sup> Sunena Tewani,<sup>1</sup> Renda Soylemez Wiener,<sup>1,2</sup> Michael Jeong<sup>1</sup>  
1-Boston Medical Center; 2-ENRM VA Hospital, Bedford, MA

**Rationale:** Studies have shown early communication with families of critically-ill patients helps to address goals of care and decrease family anxiety. We sought to increase the number of early family meetings for critically ill patients through a quality improvement initiative and to characterize the effect of early family meetings on Medical Intensive Care Unit (MICU) outcomes.

**Methods:** From February-May 2012, the Boston Medical Center MICU introduced a quality improvement initiative designed to motivate the MICU team to hold a multidisciplinary family meeting within four days of MICU admission to address goals of care for critically ill patients with metastatic cancer and those status post cardiac arrest. The quality initiative included staff meetings to discuss rationale for early family meetings, a presentation by palliative care experts discussing meeting techniques, a new EMR template to guide family meeting agenda, regular email reminders to staff, and fliers around the ICU identifying triggers for family meetings. We used a pre-post design to compare outcomes for MICU patients meeting the triggers for the 6 months before versus the 6 months after the initiative was introduced.

**Results:** There were no differences between pre (n=105) and post intervention (n=87) groups in regards to age, sex, or race. The pre group had fewer patients originating from a skilled nursing facility (15.2% vs 31%, p=0.009). After the intervention, there were significantly more family meetings within the first 4 days for patients with metastatic cancer or cardiac arrest (33.3% vs 62.1%, p<0.0001), and significantly more patients who had a code status change leading to either de-escalation or no further escalation of care (32.4% vs 48.3%, p=0.02). There was a trend towards more palliative care consults after the intervention (21.9% vs 33.3% p=0.08). However, there was no difference in median length of stay in the MICU (3 vs 3, p=0.54) or hospital (8 vs 7, p=0.47), hospital mortality (36.2% vs 40.2%, p=0.57), 30-day readmission rate (32.8% vs 23.1%, p=0.24) or median number of days of non-beneficial resource utilization (2 vs 3, p=0.79).

**Conclusion:** Our quality improvement initiative resulted in a greater proportion of patients with advanced cancer or cardiac arrest receiving early family meetings to address goals of care, resulting in changes in code status and a trend towards more palliative care consults. Further studies with a larger number of patients are required to assess whether early family meetings results in changes in other ICU outcomes.

## Category: Quality Improvement / Education

### Non-invasive imaging for cardiac amyloidosis — Delaying the obvious?

Ashley Brogan, Yanli Ding, David R. Pimentel, Flora Sam

**Introduction:** An 81 year old Hispanic man with a prior history of hypertension, atrial fibrillation, and heart failure (HF) with preserved ejection fraction presented to his cardiologist for follow up after multiple hospitalizations for presyncope, COPD exacerbation and acute HF. Echocardiogram, electrocardiogram, and the patients symptoms were concerning for amyloidosis.

**Case Description:** A complete work up was done including a fat pad biopsy which was highly positive for Congo red staining and immune gold testing was positive for the amyloid fibrils, lambda light chain (AL) immunoglobulins. There was no labeling observed for secondary (AA) or amyloidogenic transthyretin (ATTR), and serum variant ATTR screening was negative. As worsening renal function precluded cardiac magnetic resonance (CMR), a 99mtechnetium (Tc)-pyrophosphate scan was performed to differentiate between ATTR and AL amyloidosis. This showed increased uptake of the radiotracer in the heart compared to the chest at a ratio of 1.67, implying ATTR amyloidosis. , a bone marrow biopsy was performed which showed 60% cellularity. Immunohistochemistry (IHC) studies demonstrated CD138 staining of aggregated plasma cells (approximately 15% of cellularity) with a predominance for lambda AL immunoglobulin staining consistent with a plasma cell dyscrasia and AL amyloid.

**Discussion:** This case explores the challenges of differentiating the multiple forms of cardiac amyloidosis. Amyloidogenic Transthyretin Wild-type (ATTRwt) cardiac amyloidosis (also known as senile systemic amyloidosis or age-related amyloidosis) was thought most likely, given the patient's age and persistent HF symptoms of 2 years. However, his echocardiogram did not reveal marked LVH, which is a common finding with ATTRwt. The use of 99mTc-pyrophosphate to differentiate AL from ATTR using both semi-quantitative and quantitative methods has recently been described. ATTR patients had a higher semi-quantitative visual score and quantitative score (97% sensitivity and 100% specificity) vs. AL amyloidosis patients. However, his biomarkers, fat pad and bone marrow biopsy indicated AL amyloid. We believe that this is the first case, using these criteria, to demonstrate that significant 99mTc-pyrophosphate tracer uptake can also occur in AL patients. In conclusion, we present a case of a patient afflicted with AL cardiac amyloidosis with positive cardiac 99mTc-pyrophosphate imaging. This highlights the challenge in differentiating the forms of amyloid and in particular the difficulty of diagnosing ATTRwt cardiac amyloidosis.

## **Category: Quality Improvement / Education**

### **The Fungus Among Us: A Rare Rash in a non-HIV Patient**

**Myfanwy Callahan and Raagini Jawa**

**Introduction:** Opportunistic fungal infections are frequently observed in immunocompromised patients, noted most often in HIV-infected patients, transplant recipients, or those receiving chemotherapy. This unusual infection found in a patient with sarcoidosis demonstrates the importance of remaining vigilant to opportunistic infections in anyone receiving immune-suppressant medication.

**Case Description:** The patient is a 61 year old man with a history of sarcoidosis affecting the heart, liver, and bones, which had been treated with infliximab, methotrexate, and chronic prednisone. He presented with a rash on the right scapula which had been present for two months. Initially it erupted as two small lesions. When it did not resolve he presented to his primary physician who referred him to dermatology. Several weeks later the two lesions had grown significantly. At this time a biopsy was performed showing the skin infection to be cryptococcal. He was admitted to evaluate him further for disseminated Cryptococcus. His only symptoms were the rash, a mild headache and dry cough without fever or meningeal signs. Physical exam was notable for a 12cm confluent mass of erythematous papules over the right scapula. CT of the thorax revealed new ground glass opacities in the left lung in this patient with no prior lung manifestations of sarcoidosis. He underwent a lumbar puncture and bronchoscopy to rule out cryptococcal meningitis and pulmonary Cryptococcus. Blood samples and cerebrospinal fluid (CSF) were negative for Cryptococcal antigen and fungal cultures of blood, however bronchial lavage did eventually return positive for Cryptococcus. He was discharged on fluconazole for a six- to twelve-month taper.

**Discussion:** Cryptococcus neoformans is a yeast present in the environment and found in soil. The usual port of entry is the respiratory tract, and it can lay dormant in immunocompetent hosts. Immunocompromised hosts, such as those with AIDS, on chronic immunosuppressants, and transplant recipients are particularly at risk for reactivation and dissemination of this infection which can have life-threatening clinical consequences such as meningoencephalitis. Cryptococcal skin lesions are usually due to hematogenous dissemination (ie: secondary cutaneous Cryptococcus). Case reports of primary cutaneous Cryptococcus have been present since the 1950's where the presumed port of entry is direct inoculation into the skin. However, these are controversial as it is generally believed that isolated cutaneous lesions cannot exist without previous, current, or delayed systemic involvement. This case of a cryptococcal skin lesion emphasizes the importance of monitoring patients on immune-suppressant therapy for opportunistic infections, and further the importance of evaluating patients with any cryptococcal infection for systemic involvement.

## **Category: Quality Improvement / Education**

### **Improving the Diagnostic Workup and Management of Type II HIT**

Enrico Castellucci, Michelle Chung, Mark Nazal, Youssef Rahban, Mark Sloan

**Aim and Goals:** The aim is to increase awareness and recognition of HIT and the 4T Score in our academic medical center with the goals of improving patient safety, increasing the quality of care, and increasing cost-effectiveness.

**Background:** Type II Heparin-Induced Thrombocytopenia (HIT) is an under-recognized life threatening prothrombotic drug reaction caused by exposure to heparin, regardless of dose or route of administration. The delayed recognition and improper diagnostic workup and management of HIT contribute to adverse patient outcomes, as well as increased costs for the patient and healthcare system. Poor outcomes related to HIT are also a known area of medical malpractice litigation.

**Setting:** Boston Medical Center (BMC)

**Methods:** A total of 176 patients admitted to Boston Medical Center in 2012 underwent HIT ELISA testing. Of these, a random sample of 50 patients was selected for chart review. Patients were retrospectively assigned a 4T score and subsequent analysis was done of the diagnostic workup sequence and management steps. In addition, a brief survey looking at current knowledge of the appropriate management of HIT was sent to 157 Internal Medicine Residents at Boston Medical Center with 58 respondents (37%).

**Results:** Retrospective patient analysis revealed that 40% had a 4T score categorized as Low Clinical Suspicion, which would indicate that HIT ELISA testing was unnecessary. When compared to evidence based workup protocols the majority of patients (90%) had diagnostic tests ordered in incorrect sequence or unnecessarily. In these patients where HIT was suspected the use of Doppler ultrasound to diagnosis thrombosis and the use of alternative anticoagulation was erroneously omitted in 75% of cases. Of the residents surveyed at BMC approximately half (48%) did not know all components of the 4T score and a minority (7%) indicated they would ‘always’ order Doppler ultrasound when HIT is suspected.

**Conclusions:** Despite evidence-based literature demonstrating the utility of the 4T score and the management of Type II HIT, a gap remains in awareness. This leads to inappropriate testing and management of patients at risk of poor outcomes related to this prothrombotic drug reaction.

**Recommendation/Future Intervention:** An integrative HIT Order Set implemented in Boston Medical Center’s electronic medical record system could improve diagnostic workup and management of HIT. This incorporates an embedded 4T score with recommended test sequence as well as orders for diagnostic tests and an alternate anticoagulant when indicated.

## Category: Quality Improvement / Education

### Hypercalcemia associated with mineral oil-induced granulomas

Kim Chiang, MD

Mentor: Nadine Palermo, MD

**Introduction:** Hypercalcemia can occur in granulomatous diseases, such as sarcoidosis and tuberculosis. In these conditions, there is increased intestinal calcium absorption induced by high serum calcitriol levels (1,25-dihydroxyvitamin D). In healthy subjects, the conversion of 25-hydroxyvitamin D (calcidiol) to calcitriol occurs via a 1-hydroxylase (CYP27b1) in the kidney proximal tubule. This process is normally regulated by parathyroid hormone (PTH), which is suppressed in the setting of hypercalcemia. However, in sarcoidosis and other granulomatous disorders, activated mononuclear cells (especially macrophages) produce calcitriol from calcidiol independent of PTH, via the autonomous activity of CYP27b1.

**Case Description:** A 35 year-old man presented with recurrent symptomatic hypercalcemia. He has a history of intramuscular Synthol injection use (a mineral oil based product that creates the appearance of muscle bulk) for body building purposes. His last use was 2 years prior to presentation. His physical exam was notable for multiple raised, hardened plaques over the bilateral deltoids, biceps, and pectoralis major. These were thought to be reaction-granulomas (paraffinomas) at the sites of mineral oil injection. His labs demonstrated a total calcium of 15.2, a free calcium greater than assay (>7.8), a phosphorous of 2.3, and a creatinine of 2.25. His intact PTH was 11. His calcidiol level was below assay (<4), and his calcitriol level was 101. His angiotensin-converting enzyme (ACE) level was 85. TSH was within normal limits. His chest x-ray did not show findings consistent with pulmonary sarcoidosis. The patient was admitted to an outside hospital where he received intravenous fluids until he was euvolemic. He was started on prednisone 30mg daily, and Lasix 20mg twice daily, with gradual improvement of his calcium levels to within normal range. His hypercalcemia was thought to be associated with mineral oil-induced sclerosing paraffinomas, the mechanism of which is likely due to unregulated expression of CYP27b1 by inflammatory mononuclear cells infiltrating the dermis, as in the case of sarcoidosis. He remains steroid dependent at this time.

**Discussion:** This case illustrates an unusual cause of hypercalcemia. Extensive laboratory evaluation of this patient's hypercalcemia did not suggest any of the more common etiologies. While he does have an elevated ACE level, this finding is not specific for sarcoidosis and he did not have any other signs or symptoms consistent with that diagnosis. It appears that paraffinoma-induced hypercalcemia is steroid-responsive, though the necessary duration of treatment is unclear. Unfortunately, the use of injectable liquids (most commonly mineral oil or silicone) by laypeople for cosmetic purposes is not an uncommon practice. This behavior has been observed in bodybuilders, transgendered persons, and in males seeking penile augmentation. Sclerosing paraffinomas should be considered in the differential diagnosis of hypercalcemia, especially in the presence of skin lesions suggestive of injectable liquid use.



## Category: Clinical Research

### **Inappropriate drug susceptible treatment of multidrug resistant tuberculosis patients' effects on culture conversion and final outcomes**

Pooja Chitneni, Mary W. Buckley, Julia Rohr, Danie Theron, Emily A. Kendall, Robin M. Warren, Karen R. Jacobson

**Background:** In many high burden countries, recognition of multidrug resistant tuberculosis (MDRTB) occurs weeks after initial tuberculosis (TB) diagnosis because patients do not receive drug susceptibility testing (DST) until they fail drug susceptible (DS) TB therapy and because culture-based DSTs takes weeks to produce results. While awaiting DST results, many MDRTB patients are begun on DSTB therapy. We aimed to assess whether time on DSTB treatment was associated with delayed sputum culture conversion and worse final outcomes in patients with MDRTB.

**Methods:** We analyzed a retrospective cohort of 223 patients who began MDRTB treatment between 2007 and 2010 in a rural TB hospital in the Western Cape Province, South Africa. We used Cox proportional hazards modeling from time of starting appropriate MDR treatment to culture conversion, stratifying patients by whether they received DSTB treatment for less than vs. greater than one month after having an MDRTB positive sputum culture collected. DSTB treatment was defined as being on isoniazid, rifampicin, ethambutol, and pyrazinamide. We performed logistic regression analysis to evaluate the association between time on DSTB therapy and final treatment outcomes; good outcomes included treatment completion and transfer out in good condition, and poor outcomes included treatment failure, death, default, and transfer in poor condition.

**Results:** While on MDRTB therapy, 202 patients (90.6%) converted their cultures to negative. Mean time to culture conversion was 1.57 months. In univariate analysis, being on inappropriate DSTB treatment for greater than one month was associated with longer culture conversion times (adjusted HR=0.76 [0.57-1.01]  $p=0.056$ ). There was no significant difference in likelihood of poor treatment outcomes at 24 months between patients on inappropriate first line treatment for more than one month compared to those on inappropriate treatment for less than 1 month (unadjusted OR=1.39 [0.82-2.36]  $p=0.230$ ).

**Conclusion:** Our data suggests that for MDRTB patients there is a trend toward delayed culture conversion in patients who received more than one month of inappropriate DSTB therapy. Future treatment algorithms will need to consider whether starting patients on empiric therapies with delays until DST is available may worsen short and long term outcomes, and future studies need to examine whether there is a time threshold before these inappropriate empiric therapies have an impact.

## Category: Clinical Research

### Risks and benefits of large volume paracentesis in spontaneous bacterial peritonitis with tense ascites; Where is the clinical evidence?

Ehsan Chitsaz MD, MHSc, David Nunes, MD

**Background:** Spontaneous bacterial peritonitis (SBP) is the most common bacterial infection in cirrhosis with high mortality. Antibiotics are the mainstay of treatment. Moreover, albumin infusion in SBP improves survival by 60% and decreases the risk of acute renal impairment.

Large volume paracentesis (LVP) is the standard treatment for tense ascites. LVP is historically avoided in patients with SBP due to the potential risk of circulatory dysfunction. These are based on presumed physiologic mechanisms and have not been adequately studied with robust clinical outcomes.

**Aims:** We decided to determine whether or not LVP can be safely used in SBP patients, especially in the era where albumin infusion, regardless of performing LVP or not, is part of SBP management. Potential benefits of LVP in SBP include: improved patients' abdominal discomfort, decreased ascites microbial load, decreased intra-abdominal pro-inflammatory cytokines, and bacterial vasoactive peptides. Potential risks of LVP in SBP include circulatory dysfunction due to fluid shift and extravasation; and risks of removing ascites protein contents including humoral immunity molecules, complement cascade peptides, and opsonins.

**Methods:** We conducted a systematic review of randomized controlled clinical trials (RCTs). We searched Medline, EMBASE, Cochrane CENTRAL, and Clinicaltrials.gov databases using controlled vocabularies (MeSH, Emtree), and key word searching for large volume / therapeutic paracentesis, spontaneous bacterial peritonitis, and refractory/ tense ascites. We also screened all SBP trials as well as all LVP trials. We also performed hand searching and cross referencing of clinical guidelines and major reviews.

**Results:** Our comprehensive search retrieved 189 trials in Medline, 147 in Cochrane CENTRAL, 91 in EMBASE, and 28 in Clinicaltrials.gov in English. After removing the duplicates there was only randomized controlled clinical trial that studied LVP in SBP patients. All other LVP trials had excluded SBP patients from their studies. Similarly, all SBP trials did not include LVP in their management. The AASLD clinical guidelines did not provide recommendations regarding whether or not LVP can be considered in SBP. The only available RCT of LVP in SBP randomized 42 SBP patients to receive LVP (group 1) vs no LVP (group 2). 12 months survival was not statistically significantly different between two groups (11.1% vs 14.3%,  $P > 0.05$ ), however symptoms resolved faster with LVP ( $P = NS$ ) but with slightly higher rate of renal impairment ( $P = NS$ ).

**Conclusion:** There is an extreme paucity of evidence with regard to role and safety of LVP in tense ascites in SBP. The current clinical guidelines do not provide recommendations on whether or not LVP can be considered in SBP. The only retrieved small RCT showed no worse outcomes with LVP, whereas LVP may cause faster symptom relief.

**Future Efforts:** We suggest that well designed clinical trials that are sufficiently powered, and with the optimal albumin infusion (based on the current guidelines) be conducted to further elucidate the role and safety of large paracentesis in SBP.

## **Category: Senior Talk**

### **Developing Tools to Improve Medication Reconciliation**

Kevin deHaan, MD

There are at least 1.5 million adverse drug events every year in the United States. Two-thirds of inpatients have at least one medication discrepancy. Many of the clinically significant discrepancies result from errors in obtaining the best possible medication history. Medication errors are implicated in prolonged admissions and increased risk of complications which result in an estimated \$80 billion per year of healthcare spending. The Multicenter Medication Reconciliation Quality Improvement Study (MARQUIS) trial is currently evaluating interventions across six sites in the US. A toolkit, including medication history pocket guides, from the MARQUIS trial guided the investigation and development of tools for BMC.

There are many challenges to obtaining a best possible medication history. Swim lane diagrams were constructed to evaluate work flow for an average medicine admission at BMC. A fishbone diagram was constructed to identify obstacles at BMC. Obstacles include lack of education of providers and gaps in electronic medical record integration on top of patient factors such as poor education, language barriers, and polypharmacy. Educational tools developed by the MARQUIS investigators were modified to the work flow at Boston Medical Center (BMC). To bridge these gaps, I propose educational initiatives and tools for incoming interns to assist in obtaining a best possible medication history. Additionally, pharmacist or pharmacy technician support in obtaining medication history, may be beneficial, especially for high risk patients.

## Category: Basic Research

### Multi-Host Approach for the Systematic Analysis of Virulence Factors in *Cryptococcus neoformans*

Athanasios Desalermos<sup>1</sup>, Xiaojiang Tan<sup>2</sup>, Rajmohan Rajamuthiah<sup>2</sup>, Marios Arvanitis<sup>1</sup>, Yan Wang<sup>2</sup>, Dedong Li<sup>2</sup>, Themistoklis K. Kourkoumpetis<sup>1</sup>, Beth Burgwyn Fuchs<sup>2</sup>, and Eleftherios Mylonakis<sup>2</sup>

1. Department of Internal Medicine, Boston Medical Center, Boston University School of Medicine, 2. Division of Infectious Diseases, Rhode Island Hospital, Warren Alpert Medical School of Brown University

**Introduction:** *Cryptococcus neoformans* is a fungal pathogen that primarily infects the lungs and the central nervous system. Vertebrate models for the study of cryptococcal pathogenesis raise ethical and logistical concerns. Invertebrate model hosts, such as the nematode *Caenorhabditis elegans* and the insect *Galleria mellonella*, can be used to study fungal pathogenesis. Notably, key virulence factors that are important for cryptococcal pathogenesis in invertebrate are also involved in pathogenesis in humans.

**Methods:** A multi-host approach was followed to screen a library of 1201 signature-tagged deletion strains of *C. neoformans* mutants to identify previously unknown virulence factors. The primary screen was performed using a *C. elegans* – *C. neoformans* infection assay. The hits among these strains were reconfirmed as less virulent than the wild type in the insect *G. mellonella* – *C. neoformans* infection assay. After this 2-stage screen, and to prioritize hits, we performed serial evaluations of the selected strains, using the *C. elegans* model. All hit strains identified through these studies were validated in a murine model of systemic cryptococcosis. We confirmed that each strain identified as a hit strain represents a deletion in the gene of interest by PCR with the use of tag-specific primers. To characterize the functional role of the identified genes in *C. neoformans* pathogenesis, we performed a series of in vitro assays

**Results:** Among the 72 strains identified in the primary *C. elegans* screen, 50 were identified as less virulent in the *G. mellonella* model. These 50 strains were tested further in a secondary *C. elegans* screen, and 26 strains were identified. These 26 strains were then tested in a *C. elegans* model that had increasing levels of stringency. Twelve genes were identified through the stepwise screening assay. Among them, 4 (*CSN1201*, *SRE1*, *RD11*, and *YLR243W*) were previously discovered, providing proof of principle for this approach, while the role of the remaining 8 genes (*CKS101*, *CNC5600*, *YOL003C*, *CND1850*, *MLH3*, *HAP502*, *MSL5*, and *CNA2580*) were not previously described in cryptococcal virulence. Interestingly, we identified 10 genes that appear to affect melanin. Melanin is a crucial virulence factor for *C. neoformans*.

**Conclusion:** We developed and performed a stepwise screening assay. Previous screening efforts in alternative hosts primarily involved a single model host on studying a relatively small number of pathogenic strains. The novelty of the current system is that we have systematically infected different model systems, *C. elegans*, *G. mellonella*, and mice, of increasing complexity in both physiology and ease of handling. Our hypothesis was that genes required for virulence in multiple hosts with different conditions possibly are important to pathogenetic capability. The additional hosts added complexity in our screen by exploring additional pathways in hosts with increasingly sophisticated immune systems. Interestingly, all 12 strains predicted through our screens in invertebrate hosts were associated with mammalian infection. Our findings and approach could provide helpful insights to researchers planning large pathogenesis screens.

## Category: Clinical Research

### Culture if spikes? Not so fast.

Muhammad Dhanani, Katherine Linsenmeyer, Kalpana Gupta, Judith Strymish, Anthony C. Breu

**Background:** Given the high mortality associated with untreated bacteremia, physicians have a low threshold to obtain blood cultures for patients on acute care wards. Most studies on blood culture ordering include patients in the emergency department, limiting our understanding of true positivity and indications for cultures drawn on hospitalized patients. We sought to identify the yield and self-reported indication for blood cultures ordered during inpatient stays.

**Methods:** All blood culture orders written by inpatient providers on a general medicine service from 10/1/14 to 2/11/15 and 3/9/15 to 4/15/15 were reviewed for patient characteristics, indication, and positivity on a daily basis. As part of the electronic order, providers selected from among a list of indications for the blood culture order. Classification of positive blood cultures into true and false positive was determined by consensus among staff at VA Boston's microbiology and infectious disease departments. A blood culture order was defined as an electronic entry and included all sets drawn as a result of that order.

**Results:** During the study period, providers placed a total of 476 orders, of which 20 (4.2%) included 1 set of blood cultures and 437 (91.8%) included 2 sets. Eighteen orders resulted in true positive cultures (3.8%) and twelve resulted in false positive cultures (2.5%). The most common indications were fever (43.5%; mean temperature 101.3 degrees Fahrenheit), leukocytosis (21.4%; mean white blood cell count 14,000 with range 3,300-57,800), suspected infection (28.2%), and follow-up of previously positive cultures (16.6%). For the 207 patients with fever as a listed indication, 6 cultures resulted in true positives while 6 cultures resulted in false positives; 115 patients had fever as the only listed indication, and 3 of these patients had true positive blood cultures while 4 had false positive blood cultures. The combination of fever and leukocytosis occurred in 59 patients and was associated with 3 true positives and 3 false positives.

**Conclusions:** The rate of true positive blood cultures among hospitalized patients was notably lower than previously published true positive blood culture rates of greater than 10% when emergency medicine patients are included. Fever among patients on an acute care inpatient ward yielded few true positive blood cultures, suggesting fever spike alone is not a robust indication for ordering blood culture. Fever in combination with leukocytosis has a similar predictive value to fever alone. More research is needed to determine which indications for blood cultures have the greatest yield.

## Category: Quality Improvement / Education

### A Rare Cause of Renal AA Amyloidosis

Bitu Fakhri M.D.<sup>1</sup>, Lauren Stern M.D.<sup>2</sup>

<sup>1</sup>Boston University School of Medicine, Internal Medicine Residency Program, Boston, MA 02118

<sup>2</sup>Boston University School of Medicine, Renal Section, Boston, MA 02118

**Introduction:** Serum Amyloid A (AA or secondary) amyloidosis is an unfortunate and rare complication of chronic inflammatory disease. This condition develops when proteolytic fragments of the acute phase reactant, serum amyloid A (SAA), are deposited into tissue as amyloid fibrils. Amyloid deposits throughout the body can then lead to a progressive deterioration in organ function. A number of conditions have been well known to be associated with secondary amyloidosis, but systemic sarcoidosis has rarely been mentioned in the literature in association with this condition. We present a case in which AA amyloidosis was found to be secondary to systemic sarcoidosis.

**Case Description:** A 64 year old African-American woman with past medical history significant for well-controlled diabetes mellitus, hypertension, and systemic sarcoidosis was referred to nephrology clinic for evaluation of new onset proteinuria. A kidney biopsy was performed and revealed AA amyloidosis as the etiology of her nephrotic syndrome. An extensive workup was performed to identify the etiology of secondary amyloidosis due to its very rare association with sarcoidosis. After the most common causes were ruled out with convincing clinical and laboratory evidence, sarcoidosis was determined to be the cause of AA amyloidosis.

**Discussion:** A number of conditions are well known to be associated with secondary amyloidosis. These includes chronic inflammatory conditions such as rheumatoid arthritis, familial periodic fever syndromes, psoriasis, inflammatory bowel disease; malignancies such as renal cell carcinoma and Hodgkin's lymphoma; chronic infections including tuberculosis, chronic osteomyelitis, and cellulitis from subcutaneous injection of illicit drugs. There are also a number of cases which have no identifiable cause of secondary amyloidosis. The mainstay of treatment in AA amyloidosis is controlling the underlying disease, and thus reducing the production of serum Amyloid A protein. Antibiotics and colchicine are effective at treating and preventing infection related and familial Mediterranean fever-related AA amyloidosis, respectively. Recently, TNF-alpha blockers have emerged as effective agents in AA amyloidosis associated with some autoimmune disease. Eprodisate, a new agent, binds to the glycosaminoglycan binding site on amyloid fibrils, thus targeting amyloid fibril polymerization and tissue deposition. The results of a recent randomized trial showed that eprodisate may slow the decline of renal function in AA amyloidosis and confirmatory studies are underway.

**Category: Quality Improvement / Education**

**The Role of Induction Chemotherapy for Head and Neck Squamous Cell Carcinoma: A Review of Literature**

Bitra Fakhri, MD, MPH; Minh-Tam Truong, MD

The addition of chemotherapy to radiotherapy (concurrent chemoradiation) is currently the modality of choice in the treatment of locally advanced head and neck squamous cell carcinoma (HNSCC) patients. However, sequential chemotherapy, in the form of induction chemotherapy followed by radiotherapy or concurrent chemoradiation, has been shown to be effective for organ function preservation, and also improve quality of life in patients with potentially resectable HNSCC. A review of trials using platinum and 5-fluorouracil (PF)-containing induction regimens demonstrated a significant survival benefit for this approach over locoregional treatment alone in locally advanced disease. Multiple clinical trials have been conducted to determine the most appropriate regimen for induction chemotherapy prior to chemoradiation. In recent years, the introduction of taxanes into induction chemotherapy has provided physicians with more effective regimens. The triplet combination induction regimen of docetaxel, cisplatin, and 5-fluorouracil (TPF) has proved to be more efficacious in prolonging survival than the doublet PF. Current trials, comparing TPF induction chemotherapy versus targeted therapies (cetuximab) have not shown any statistically significant difference between the two regimens in terms of mortality and progression-free survival.

## **Category: Senior Talk**

### **Personalized Medicine in Oncology: The Future Is Now**

Bitu Fakhri, MD, MPH

My senior talk provides an overview of how people have understood and described cancer throughout history, as well as how the treatment of cancer has evolved.

My talk interweaves a sweeping historical narrative; with intimate stories about physicians and patients involved in the evolution of chemotherapy; and an investigation into the latest scientific breakthroughs that may have brought us, at long last, to the brink of lasting cures.

The core topics covered in my talk are as following:

- The birth of chemotherapy
- The introduction of combination chemotherapy
- The advent of adjuvant chemotherapy
- National efforts leading to discovery of new chemotherapeutic agents in the second half of the 20<sup>th</sup> century
- The dawn of targeted therapies

While we aren't yet ready to put cancer on the extinction list along with less intricate diseases, we, indubitably, face the future with less fear and frustration.



## Category: Quality Improvement / Education

### Spinal Cord Infarction after Interventional Radiology Guided Embolization for Massive Hemoptysis

Jeffrey Gerbino

Mentor: Mathew Nitzberg, Hasmeena Kathuria

**Case Presentation:** A 38 year old male with a history of prior pulmonary tuberculosis and recently diagnosed HIV was admitted with worsening hemoptysis. The patient reported previous treatment for active pulmonary tuberculosis while he was living in Africa. He had been seen by an infectious disease physician several months prior to his admission for evaluation of his HIV and was noted to have a positive quantiferon gold test. Further evaluation revealed a 10 centimeter left upper lobe cavitary lesion. At this time he did not demonstrate any active symptoms of tuberculosis. In the weeks prior to his admission he noted 1 to 2 weeks increasing volume of hemoptysis. The patient was admitted to the medical intensive care unit and shortly after developed massive hemoptysis requiring intubation, transfusion of 4 units of packed red blood cells, and emergent interventional radiology guided embolization of bronchial, internal mammary, and lateral thoracic arteries. His course was further complicated by pneumonia, left main stem thrombus, and left lower lobe collapse after bronchoscopy for clot removal. During his initial intubation and embolization, he was sedated and medically paralyzed. Once he was stabilized, sedation was lightened and it was found that the patient was unable to move his legs. His physical exam was notable for flaccid tone in his lower extremities bilaterally. He had 0/5 strength in knee flexors and extensors, plantar flexors and extensors. Absent patellar and Achilles reflex on the left. Decreased sensation to light touch and pinprick in bilateral lower extremities and absent vibratory sensation below the knees. An MRI of his spine was performed which showed a focal swelling/expansion of the cord centered at T12 level with increased T2 signal and diffusion, consistent with acute spinal cord infarct. During further evaluation to rule out other etiologies, he was noted to have renal, splenic and a cerebellar infarct. An echocardiogram did not show any evidence of vegetations or thrombi, but did show evidence of a trans-pulmonary shunt.

**Discussion:** Given the time course of events and lack of other causes, the most likely explanation for this patient's spinal cord infarct seems to be as a complication of his embolization procedure. This has been described in the literature as a potential complication of bronchial artery embolization. There may be several mechanisms that potentially occurred. One thought is that this patient may have had spinal artery feeders coming off of the bronchial artery, which were not seen on angiography. This could explain the spinal cord infarct, but not necessarily the likely embolic events seen elsewhere. With his intrapulmonary shunt, it is possible that the embolic material crossed through the shunt and entered the systemic circulation leading to the multiple embolic events seen on his CT scan.

## Category: Clinical Research

### **Epidemiology of Ventilator Associated Pneumonia and time trends of Multidrug Resistant Bacteria in the Geriatric Population**

Koukoupetis, Themistoklis<sup>1</sup>, Anagnostou, Theodora<sup>2</sup>, Arvantis, Marios<sup>1</sup>, Ziakas, Panayiotis<sup>3</sup>, Desalermos, Athanasios<sup>1</sup>, Mylonakis, Eleftherios<sup>3</sup>

1)Boston Univeristy, 2)Mount Auburn Hospital, 3) Brown University

**Background:** Ventilator Associated Pneumonia (VAP) is linked to considerable morbidity and mortality with annual cost of at least \$3.5 billion. Given the high rate of comorbidities in the elderly and their frequent hospitalizations, their microbial colonization rates can be altered and consequently affect their infection rates. To contribute to our understanding of the pathogenesis of this infection in the geriatric patients, we ventured to elucidate the differences of VAP in the elderly population.

**Methods:** We conducted a retrospective analysis of the medical charts of all 208 patients admitted to the adult medical and surgical intensive care units of a tertiary care hospital who developed VAP during a five year period. In order to evaluate the specific characteristics and outcomes of VAP in the elderly, we separated our population in two groups using the cutoff of 65 years. Group comparison was made using the Mann-Whitney non-parametric test. Count data were reported as % frequencies and compared using the Fisher's exact test. Between-group differences were adjusted by performing a multivariable logistic regression analysis, for parameters with  $p < 0.10$  at the group analysis. Adjusted effects were reported as Odds Ratio (OR) with their 95% confidence interval. Survival analysis was performed using the Kaplan-Meier method and the log-rank  $p$  statistic was reported. All tests were two-tailed, with significance level set to  $< 0.05$ . Stata v11 (College Station, TX), was used for data analysis.

**Results:** 200 patients were included in the study of which 72 (36%) were above 65 years old. Interestingly, the two populations had comparable disease severity on ICU admission (median SAPS II score 37.5 vs. 37,  $p=0.48$ ) and did not differ on other markers of illness severity such as Candida colonization (33% vs. 35%,  $p=0.82$ ). However, the older population had higher prevalence of pulmonary comorbidities (37% vs. 13%,  $p=0.005$ ) and marginally higher prevalence of diabetes mellitus (24% vs. 13%,  $p=0.08$ ). Age (HR 1.04 95% CI 1.01-1.07,  $p=0.003$ ) was an independent predictor of mortality and age  $\geq 65$  years was associated with increased incidence of VAP due to multidrug resistant bacteria (MDRB) (44% vs. 28%,  $p=0.07$ ). However, in multivariate analysis, multidrug resistant infection (HR 1.50, 95% CI 0.54-4.17,  $p=0.44$ ) was not an independent risk factor for 28-day mortality in this population. Finally, MDR VAP rates in our hospital decreased over the study period, likely as a result of the World Health Organization Guidelines regarding Hygiene measures.

**Conclusions:** Patients above 65 years old have 3 times higher mortality compared to younger adults and higher incidence of multidrug resistant bacteria.

## A multi-cultural approach to dietary restrictions in the days preceding colonoscopy

Kristin MacArthur, [Ania Leszczynski](#), Paula Quatromoni, Brian C. Jacobson

**Background:** Great variation exists in dietary restrictions prior to colonoscopy reflecting limited evidence for how specific foods effect bowel preparation. We previously demonstrated an association between dietary insoluble fiber, starch and refined grains and bowel preparation. Nonetheless, without an appreciation of foods patients prefer to consume, broad dietary restrictions prior to colonoscopy may lead to decreased compliance and lower patient satisfaction. We sought to characterize dietary preferences among a diverse population to generate evidence for a culturally sensitive approach to bowel preparation instructions.

**Methods:** We performed standardized dietary interviews with 74 patients or their family members in our endoscopy unit. We sought a minimum of 10 unrelated individuals from each of 6 national or ethnic backgrounds including US-born White (n=19, 26%), US-born African American (n=11, 15%), Haitian (n=10, 14%), Cape Verdean (n=10, 14%), Caribbean/Central or South American Latino (n=14, 19%), and Southeast Asian (n=10, 14%). We elicited information concerning commonly consumed vegetables, fruits, fish, meat, nuts, and grains, asking which foods would be most difficult to temporarily eliminate from one's diet. Soluble and insoluble fiber content of reported foods and portion sizes were computed using the Nutrition Data System for Research (NDSR) database. We used the NIH low residue diet to classify foods accordingly. We also asked subjects what they would consume if told to consume only clear liquids.

**Results:** Average subject age was 46 and 58% were male. Subjects included 29 (39%) colonoscopy patients and 45 (61%) patient family members. Only 46% were US born. The most commonly consumed foods among all cultural groups were white rice (53%), chicken (46%), beef (24%) and beans (22%). Subjects also reported these same foods would be most difficult to temporarily eliminate from their diet. Table 1 shows commonly reported foods, their fiber content, and whether they are allowed on a low residue diet. Only 72% of subjects demonstrated correct understanding of a clear liquid diet. Patients were *less* likely than family members to understand what "clear liquids" meant (62% vs 38%, p=0.01). Furthermore, 39% of subjects demonstrated incorrect understanding of "clear broth". Subjects offered cultural-specific terms to convey "clear broth" including clear soup, bouillon and consume.

**Conclusion:** We observed several commonly preferred foods among a culturally-diverse population that met criteria for a low residue diet. These foods may be suitable prior to colonoscopy without affecting bowel cleanliness. If requiring "clear liquids", very specific culturally-sensitive examples of what is acceptable should also be included in bowel preparation instructions.

## Category: Clinical Research

### Single Agent Lenalidomide Three Times a Week Induces Hematologic Responses in AL Amyloidosis Patients on Dialysis

Lichtman EI, Seldin DC, Shelton A, Sanchorawala V

**Background:** AL amyloidosis, the most common form of systemic amyloidosis, is the result of immunoglobulin (Ig) light chain production by clonal bone marrow plasma cells with subsequent widespread tissue deposition in the form of amyloid fibrils. This often results in multisystem organ dysfunction, with frequent manifestations including cardiac disease, peripheral and autonomic neuropathy, and renal failure. Clinically evident kidney disease occurs in 50-80% of patients and up to one-third of these progress to needing renal replacement therapy. The novel immunomodulatory agent lenalidomide has been incorporated into commonly used single and multidrug regimens for AL amyloidosis, but there is little experience with these agents in patients on dialysis.

**Methods:** Clinical trial of lenalidomide in patients with dialysis-dependent renal disease secondary to AL amyloidosis. All patients received lenalidomide at 10 mg orally three times a week. For those patients on hemo or peritoneal dialysis, the lenalidomide dose was given after dialysis sessions. Patients received aspirin 325mg daily (unless already on anticoagulation therapy) and proton-pump inhibitor prophylaxis. Toxicity and responses were evaluated after 1, 3, 6, 9, and 12 months of treatment. Organ responses were scored according to published criteria. Hematologic responses were based upon quantitative measures of clonal plasma cell dyscrasia and were assessed starting at 3 months after initiation of treatment.

**Results:** Seven patients were enrolled. All patients had received prior treatment, with 57% receiving prior high dose melphalan and stem cell transplantation. Two patients died before evaluation of response. The most common adverse event was infection; no thromboembolic complications were seen. One patient required dose modification. Hematologic responses were obtained by 4 of the 5 evaluable patients, with one obtaining a complete response, two obtaining a near complete response, and one obtaining a partial response. No patient developed dialysis independence, or met other criteria for organ response. Four of the 7 patients were alive with a median overall survival was 18 months. Follow up time ranged from 0.6 to 72 months from enrollment. No patient progressed to receive further treatment after completion of the trial.

**Conclusion:** Adjusted dose lenalidomide induced sustained hematologic responses in a small group of previously treated patients with AL amyloidosis on dialysis. Therapy was reasonably tolerated, although there were higher rates of adverse events than reported in those with normal renal function.

## **Category: Senior Talk**

### **Hemostatic Abnormalities in the AL Amyloid Population**

Luke Masha

Mentors: Vaishali Sanchorawala, Katherine Bever

Hemorrhage is a frequent complication of AL amyloidosis. Most commonly seen is diffuse subcutaneous bleeding. If such bleeding involves periorbital tissue (raccoon eye's sign), it is essentially pathognomonic for amyloidosis. Epistaxis and hemoptysis may also occur as a consequence of mucosal fragility. However, focal collections of amyloid fibrils (amyloidomas) may be encountered. Intra-abdominal bleeding is particularly devastating. The presentation of spontaneous hepatic, renal or splenic rupture as a consequence of marked organomegaly is highly suggestive of this disease, often recurrent, and too frequently fatal. Urologic hemorrhage has been described. However, the most prevalent, non-cutaneous bleeding site is the GI tract and both upper and lower GI pathology may be present.

Case series suggest that approximately 40% of patients with AL amyloidosis will experience clinically significant bleeding, mostly cutaneous and GI in nature. The etiology of this elevated bleeding risk is multifactorial including capillary fragility and ineffective vasodilation due to underlying autonomic dysfunction, hepatic insufficiency, and vitamin K deficiency. Rare isolated factor deficiencies (VIII, V, IX) have been described. However, the coagulopathy with the strongest correlation with clinical bleeding is an acquired factor X deficiency, occurring in approximately 10-15% of patients. Patients with a factor X level less than 50% of normal have an approximately 56% chance of a clinical bleeding event whilst deficient. The mechanism of factor X deficiency is likely binding by fixed amyloid fibrils in splenic sinusoids with evidence supporting this being the known rapid rate of clearance of infused human factor X in patients with this deficiency, as well as reports of resolution of this coagulopathy with splenectomy. Perhaps underappreciated is the notion that whilst factor X deficiency is the best recognized coagulopathy associated with AL amyloidosis, the most common is an abnormal thrombin time, occurring in 32-90% of patients. This coagulopathy is not detected with routine labs (ie PT, INR, PTT) as thrombin times mostly evaluate the fibrinogen system. Abnormal thrombin times in this population are due to either acquired fibrinogen defects or acquired thrombin inhibitors and generally only mild elevations are seen. However, some patients will develop severe bleeding due to marked abnormalities in thrombin times, often with no other identified concurrent coagulopathy.

Whilst AL amyloidosis frequently is associated with bleeding, it also is associated with thrombosis such as CVA, pulmonary embolism, critical limb ischemia, and MI. A retrospective case series regarding thrombolytic use in this population was performed. Over a 10 year period and 929 patients seen at the BMC, we identified only 4 patients who received t-PA for appropriate indications. Two patients received t-PA for acute CVA without any clinical bleeding and with good neurologic result. One patient received t-PA for acute limb ischemia which was complicated by massive GI bleeding. One patient received t-PA for a massive PE, complicated by intra-abdominal hemorrhage and death. That study also yielded insight into the nature of CVA in this patient population, with a disproportionate number of cases (eighteen out of twenty four CVA cases) being secondary to cardio-embolic sources. These findings suggest that t-PA use in non-CVA populations is fraught with complications and requires caution as AL amyloidosis patients appear at very high risk and also suggest an under-appreciation for cardiac involvement in this disease process.

## Category: Clinical Research

### Effect of helminth infection on tuberculosis disease severity

Kari R Meyer<sup>1</sup>, Steven Rios Ribeiro<sup>2</sup>, Mary Gaeddert<sup>3</sup>, Lisa Ganley-Leal<sup>3</sup>, Jerrold J Ellner<sup>3</sup>, Reynaldo Dietze<sup>2</sup>, Edward C. Jones López<sup>3</sup>, Rodrigo Ribeiro-Rodrigues<sup>2</sup>, Natasha S. Hochberg<sup>3</sup>

<sup>1</sup>Department of Medicine, Boston Medical Center, Boston, MA, United States

<sup>2</sup>Núcleo de Doenças Infecciosas (NDI), Universidade Federal do Espírito Santo (UFES), Vitória, Brazil

<sup>3</sup>Department of Medicine, Section of Infectious Diseases, Boston Medical Center and Boston University School of Medicine, Boston, MA, United States

**Introduction:** Global burden of tuberculosis (TB) remains high, with an estimated 12 million prevalent cases in 2012. There is a clear need to identify factors that alter the severity and infectiousness of TB. Recent data suggest an association between helminth infections and mycobacterial disease.

**Methods:** This pilot study aims to describe differences in TB severity in persons with TB disease and helminth infection compared to TB disease alone. We evaluated persons with suspected pulmonary TB presenting to local TB clinics in Vitoria, Brazil, and analyzed data for those with culture-confirmed pulmonary TB. We collected demographic and symptom information, sputum AFB smear and culture including colony counts, and a postero-anterior x-ray of the chest. Up to three stool ova and parasite examinations were performed for each person.

**Results:** To date, we have data on 14 people. Of these, 11 (79%) were male, the median age was 28 years (range 18-72) and four (29%) had helminths in their stool, including hookworm (n=4), *Schistosoma mansoni* (n=1), and *Strongyloides stercoralis* (n=2). Those with TB and helminth infection had more people living in their house than those with TB alone (7 vs 5.4; p=0.01). Those with TB and helminth infection also tended to have more than 200 mycobacteria on colony counts compared to those with TB alone (100% vs 50%; OR=9.00; p=0.17) and involvement of  $\geq 3$  lung zones on chest xray (100% vs 60%; OR=6.23; p=0.26), but the differences were not significant.

**Conclusion:** The small sample size limits our findings, but we have started to identify potential trends in clinical parameters between those with TB and helminth infection compared to TB disease alone, with the former potentially exhibiting more severe clinical disease. Further enrollment is ongoing in order to confirm these results, achieve power to detect statistical significance, and perform multivariate analyses. If the study findings hold true, treatment of helminth infections could serve as a way to reduce the severity and infectiousness of TB disease.

## Category: Clinical Research

### Direct Access to Acute Diabetes Clinic Reduces Hospitalizations and Cost at One Year.

Marie E. McDonnell, Nadine Palermo, Katherine Modzelewski, Marina Donahue, Jennifer Britton-Colonnese, Donna Kelleher, William Baker, Sara Alexanian.

**Background:** The Emergency Department is over-utilized for both routine and acute diabetes assessment, resulting in unnecessary hospitalization and high-cost low-quality care. The Diabetes ED Rapid Follow Up program (EDRP) at Boston Medical Center was created in 2011 by Endocrinology and Emergency Medicine to reduce unnecessary hospitalizations among diabetes patients. Patients in the ED who meet clinical criteria for rapid outpatient referral are booked directly by ED staff into unique clinic slots in the Diabetes Center occurring within 24 business hours. Patients receive multidisciplinary education and management including insulin initiation.

**Methods:** We compared subjects who showed-up for the EDRP visit with those who did not on demographic, clinical, utilization and cost outcomes.

**Results:** Of 469 patients referred over 18 months, 302 (65%) patients arrived (A), 39 (8%) cancelled (C) and 127(27%) did not arrive (NA). There was no significant difference between the groups in gender, age, health plan, time of ED discharge or time of EDRP slot, or risk factors for EDRP use. Within 6 months of referral, group A was more likely to have a follow up HbA1c than group NA (35% vs 22%  $p<0.05$ ). Of those with baseline and 6 month hemoglobin A1c (HbA1c) measurements, both groups had significant absolute mean HbA1c reduction, 2.6% (A) and 2% (NA). ED revisit at 30 days was lower in A (5%) vs. NA (15%), as was hospitalization rate, A (4%) vs. NA (15%),  $p<0.01$ . At one year, this difference in hospital use persisted, A (21%) vs. NA (41%),  $p<0.01$ . Group C was more likely to reuse the EDRP but hospitalization rate was the same as group A at one year. The estimated cost savings based on the up-front hospitalization avoidance and excess hospitalization in the no-show group is \$2,819,000 annually due to reduced hospital use alone.

**Conclusions:** Our results indicate that providing open access diabetes visits to users of urgent/emergent care improves HbA1c, and those who utilize the open access service are approximately 50% less likely to be hospitalized within the next year.

## **Category: Senior Talk**

“Have you *herd*? Social media, group thinking, and health.”

Sharda Mukunda

Broadly, the objectives of this talk are to discuss social media popularity and accuracy as it relates to publicly disseminated health claims. Recent data found that about 60% of surveyed Americans look online for health information, making this a key source of perceived medical knowledge. This percentage represents a significantly larger group than in the past, in part because of increased access to the internet. Health information is also widely available on television. In particular, claims made on popular medical themed TV shows were recently found to be without rigorous scientific basis. The focus of the talk then turns to food, a topic very commonly discussed on television and on health websites. The commentary focuses on organic foods, “superfoods,” and the scientific evidence (if any) behind popular food items.



**Category: Senior Talk**

**So You Want to Run a Marathon: Risks of long-distance running**

Jordan Neviackas

Mentor: Jonathan Berz

The modern marathon has been around for over one hundred years, first run at the 1896 Olympics in Greece. Running has many benefits, however long-distance running is associated with risks. Risks range from minor to severe, including musculoskeletal, dermatological gastrointestinal, renal and cardiovascular. Current research into the cardiovascular effects of running show possible right ventricular dysfunction and risk of arrhythmias. Cardiac arrest is an uncommon occurrence, however the most common reason for cardiac arrest is hypertrophic cardiomyopathy.

## Category: Clinical Research

### **IgA anti-MPO antibodies in eosinophilic granulomatosis with polyangiitis (Churg-Strauss Syndrome)**

Esha Oommen, Amber Hummel, David Cuthbertson, Simon Carrette, Gary Hoffman, Nader Khalidi, Curry Koenig, Carol Langford, Larry Moreland, Christian Pagnoux, Philip Seo, Antoine Sreih, Peter Merkel, Dieter Jenne, Ulrich Specks, Paul Monach, For the Vasculitis Clinical Research Consortium

**Objective:** To determine the prevalence of anti-myeloperoxidase (MPO) antibodies of IgA isotype in patients with eosinophilic granulomatosis with polyangiitis (EGPA), and the association of the IgA antibodies to IgG anti-MPO and disease activity.

**Methods:** Serum samples from patients with EGPA followed in a multi-centered longitudinal cohort were tested by ELISA for the presence of IgA anti-MPO antibodies using a modified conventional assay for IgG anti-MPO. 1-2 samples per patient (300 sera from 168 patients) were tested, one sample during active EGPA and one during remission, whenever possible. Proportions of IgA anti-MPO positive samples were compared between 87 healthy controls and: 1) all patients with EGPA, 2) samples from periods of active EGPA, 3) samples from periods of relatively high activity, and 4) high activity off treatment. Clinical manifestations were compared between IgA-positive and IgA-negative patients.

**Results:** The ELISA showed low background readings in controls and high readings in some EGPA samples, and was therefore interpretable. IgA anti-MPO was detected in 11 of 168 (7%) patients with EGPA (12 of 300 serum samples) compared to 1 of 87 (1%) healthy controls ( $p = 0.067$ ). All but one (11 of 12) samples testing positive for IgA anti-MPO also tested positive for IgG anti-MPO. In contrast, 90 of 101 samples tested positive for IgG anti-MPO but negative for IgA. Samples taken during active EGPA were positive for IgA anti-MPO in 6 of 64 cases (9%,  $p = 0.042$ ). Among samples taken during relatively high disease activity (physician global assessment  $> 3$  on a scale of 0-10), 5 of 40 were positive (13%,  $p = 0.012$ ). Among the samples reflecting high activity, only two were taken from untreated patients, but both were positive for both IgA and IgG anti-MPO. No significant differences ( $P > 0.108$ ) in the rates of historical ENT, pulmonary, or skin involvement were detected between the IgA anti-MPO positive and negative patients.

**Conclusions:** Although IgA anti-MPO is detectable in some patients with EGPA and may be detectable more frequently during active disease, its presence seems unlikely to assist with diagnosis or determination of disease activity above what is obtained from conventional IgG anti-MPO. Further study of more untreated patients with active disease is indicated to determine whether IgA anti-MPO has potential clinical utility.

**Category: Senior Talk**

**Extreme Makeover: Primary Care Edition**

Tom Peteet

The purpose of my senior talk is to introduce an example of primary care redesign and to engaged residents and faculty in applying new models of primary care to their work at Boston Medical Center. The talk is based on my experience with Iora Health in New York. Iora Health is a for-profit organization founded by physician Rushika Fernandopulle aimed at transforming primary care delivery through streamlined EMR, integrative behavioral health, and health coaching for all patients. Iora Health has demonstrated significant improvement in hypertension and diabetes management, as well as exemplary patient satisfaction scores. The talk asks residents three major questions in light of Iora's success. First, what is the ideal job for a physician in the 21<sup>st</sup> century? Second, how can we reorganize clinical services and staffing to address the underlying causes of disease in our patients? Third, how can we advocate for meaningful changes to EMR's and health policy to incentivize clinical innovation, as opposed to redundant documentation?

## **Category: Senior Talk**

### **The History of Diabetes Mellitus: A Sweet Perspective**

Silpa Poola Kella

Diabetes mellitus (DM), a disease that now affects approximately 382 million individuals worldwide, has been documented for over 3000 years. Dating back to the ancient Egyptians, Ebers Papyrus describes the condition as "too great emptying of the urine." It was not until the ancient Greek physician by the name of Apollonius of Memphis coined the term, "diabetes" which means to go through or to siphon. Nineteenth century brought about important discoveries in physiology. At this time, Claude Bernard performed a series of experiments that proved that the glycogen storage occurs in the liver and blood glucose control is regulated by both the liver and dietary carbohydrate. The pathogenic link between pancreas and DM was elucidated in 1889 by Oscar Minkowski and Joseph Von Mering after they induced DM in pancreatectomized dogs. However, it was not until 1921 when a team consisting of Frederick Banting, John JR McLeod, Charles Best and James Collip isolated insulin from pancreatectomized dogs. This discovery, which led to Banting and McLeod winning the Nobel Prize in Medicine in 1923, revolutionized diabetes treatment for patients around the world. In 1937, Sir Herald Pervical Hemsworth, a British physician, was the first to differentiate between insulin sensitive and insulin-resistant individuals which paved the way for further studies differentiating Type I and Type II DM. Discoveries of guanidine in 1918 and sulfonylureas in 1942 brought the age of oral agents in the battle against diabetes. Attempts to cure DM through pancreatic transplant and islet cell transplantation were introduced in the 1960s and 1970s. With the onset of these treatments, glycemic control gained importance in medicine. The observation by Samuel Rahbar in 1965 of an abnormally fast hemoglobin fraction in DM patients that was identical to the HbA1c revolutionized how we view glycemic control. As we move through time, landmark trials including the DCCT (Diabetes Control and Complications Study) and the UKPDS (United Kingdom Prospective Diabetes Study) proved intensive glycemic control in both Type I and Type II DM decreased the risk of end organ complications. The DPP (Diabetes Prevention Program) proved lifestyle modification with diet and exercise decreased the risk of developing DM. With our ever-expanding clinical knowledge, the DM epidemic continues to grow in part to globalization with predictions of approximately 600 million individuals with DM by 2035. Policy changes aimed at changing dietary behavior such as the Soda Tax passed in 2014 in Berkeley, California aim to decrease the prevalence of the disease. In addition to policy, new technology aims to improve outcomes for patients. The bionic pancreas which is the first closed loop insulin and glucagon delivery system has shown marked improvement in blood sugar control compared to standard therapy in preliminary studies. As we move forward, we will continue to build on our understanding of DM to further the prevention and treatment of the disease.

## Category: Clinical Research

### Metabolic syndrome is associated with preclinical alterations in myocardial microstructure

Youssef Rahban, Harpaul Sandhu, Courtney Donohue, Pranoti Hiremath, Susan Cheng, Wilson S. Colucci, MD, and Jennifer E. Ho, MD

**Background:** Metabolic syndrome (MetS) is thought to lead to myocardial fibrosis and can precede diastolic dysfunction and heart failure with preserved ejection fraction. Thus far, noninvasive assessment of cardiac fibrosis has not been evaluated in a preclinical population without known cardiovascular disease. We evaluated alterations in myocardial microstructure in individuals with MetS using a novel algorithm to analyze ultrasonic backscatter applied to standard echocardiographic images.

**Methods:** A total of 162 subjects with MetS without known cardiovascular disease, 47 obese controls without MetS, and 45 non-obese controls underwent standard cardiac echocardiography. A novel validated computational backscatter algorithm was used to investigate myocardial microstructure based on sonographic signal intensity and distribution. The associations of the Signal Intensity Coefficient (SIC, measure of left ventricular microstructure) and the myocardial structural index (MSI, SIC corrected for relative wall thickness) with MetS status were determined using analysis of covariance.

**Results:** Among 254 participants, mean age was  $42 \pm 11$  years, and 75% were women. Both SIC and MSI were significantly higher in individuals with MetS compared with the obese (SIC and MSI  $p < 0.001$ ) and non-obese groups (SIC  $p = 0.04$ , MSI  $p < 0.001$ ). These findings remained statistically significant after adjustment for potential confounders, including age, sex, body mass index, systolic blood pressure, anti-hypertensive treatment, diabetes mellitus and triglyceride to HDL cholesterol (TG/HDL) ratio ( $p < 0.05$  for all). No significant difference in SIC or MSI was observed between obese and non-obese controls. There was a significant positive correlation between SIC and both triglyceride concentrations ( $r = 0.21$ ,  $P = 0.0007$ ) and the triglyceride-to-HDL cholesterol ratio ( $r = 0.2$ ,  $P = 0.001$ ). Diastolic function as assessed by the e' tissue Doppler mitral annular velocities, the mitral early wave to e' ratio, and the spectral Doppler mitral inflow pattern was significantly impaired in individual with MetS ( $P < 0.05$  for MetS vs controls and MetS vs obese).

**Conclusion:** Our findings suggest that preclinical MetS and specific features of metabolic disease are associated with altered myocardial microstructure. In previous studies, higher SIC and MSI have been associated with greater extent of fibrosis in hypertension. This study suggests that ultrasonic backscatter may reflect preclinical fibrosis in MetS. Early detection of microstructural changes may enable future targeted preventive efforts in metabolic disease.

## Category: Clinical Research

### Atrial flutter – clinical correlates and adverse outcomes in the Framingham Heart Study

Rahman F, Wang N, Yin X, Ellinor PT, Lubitz SA, LeLorier PA, McManus DD, Benjamin EJ, Magnani JW.

**Introduction:** Few epidemiological cohort studies have evaluated atrial flutter (flutter) as an arrhythmia distinct from atrial fibrillation (AF). We examined the clinical correlates of flutter and its associated outcomes to distinguish them from those associated with AF in the Framingham Heart Study.

**Methods:** We reviewed and adjudicated electrocardiograms previously classified as flutter or AF/flutter and another 100 electrocardiograms randomly selected from AF cases. We examined the clinical correlates of flutter by matching up to 5 AF and 5 referents to each flutter case using a nested case-referent design. We determined the 10-year outcomes associated with flutter with Cox models.

**Results:** During mean follow-up of  $33.0 \pm 12.2$  years, 112 participants (mean age  $72 \pm 10$  years, 30% women) developed flutter. In multivariable analyses, smoking (odds ratio [OR] 2.84; 95% confidence interval [CI], 1.54 to 5.23), increased PR interval (OR 1.28, per SD; 95% CI, 1.03 to 1.60), myocardial infarction (OR 2.25; 95% CI, 1.05 to 4.80) and heart failure (OR 5.22; 95% CI, 1.26 to 21.64) were associated with incident flutter. In age- and sex-adjusted models, flutter (vs. referents) was associated with 10-year increased risk of AF (hazard ratio [HR] 5.01; 95% CI, 3.14 to 7.99), myocardial infarction (HR 3.05; 95% CI, 1.42 to 6.59), heart failure (HR 4.14; 95% CI, 1.90 to 8.99), stroke (HR 2.17; 95% CI, 1.13 to 4.17), and mortality (HR 2.00; 95% CI, 1.44 to 2.79).

**Conclusions:** We identified the clinical correlates associated with flutter and observed that flutter was associated with multiple adverse outcomes. Future studies may clarify how flutter treatment modifies its prognosis.

## **Category: Senior Talk / Medical Grand Rounds**

### **On Track to Managing the HCV and Opiate Abuse Epidemics: Engaging Active Injection Drug Users in Primary Care**

Pooja R. Ravall<sup>1</sup>, Jonathan Pincus<sup>2</sup>

1. Internal Medicine , Boston University Medical Center, Cambridge, MA
2. Internal Medicine, Codman Square Community Health Center, Dorchester, MA

**Statement of Problem or Question:** Active injection drug users, a marginalized population typically not engaged in primary care, have high utilization of urgent healthcare resources and the major drivers of the dual epidemics of hepatitis C and overdose deaths in Massachusetts.

**Objectives of Program/Intervention:** To prevent transmission of Hepatitis C by treating patients with HCV and ongoing injection drug use. To utilize a Community Health Worker (CHW) model to retain high-risk patients in care. To link public health substance abuse programs (needle exchanges) to community health centers (CHCs) to engage a marginalized population in medical substance abuse treatment and primary care.

**Description of Program/Intervention:** The Innovations Clinic (named for the Thomas M. Menino Innovations in Primary Care Challenge Grant) uses a CHC as the medical home to engage active injection drug users infected with HCV. Patients are screened at two needle exchange programs in the Boston area and connected to a CHW, who facilitates linkage to the health center within days. The program is a low barrier, open-access outpatient buprenorphine treatment program with weekly visits to engage participants in substance abuse, primary care, and mental health services. Other CHC resources, including ophthalmology, dental, specialty referrals, social services and behavioral health are available to participants at their visits. When patients are stabilized on buprenorphine, HCV infection is treated using direct acting antivirals. The CHW assists with social issues including housing, transportation, accessing community resources, and adherence to HCV therapy.

**Measures:** The metrics to track engagement in care are: retention in care, preventive healthcare including immunizations & cancer screening, STI screening and treatment, visits for other medical problems, and rates of ED and hospitalizations in the year prior to and during our intervention. We track performance on HCV disease specific measures: HAV and HBV immunity, HCV evaluation (genotype, fibrosis markers, and Fibroscan), start, completion and adherence to treatment, and sustained virologic response. Rates of opiate abstinence are measured by weekly patient report and urine and oral swab monitoring. We also evaluate qualitative data, including patient perceptions of addiction & liver disease, and social determinants of health and barriers to care prior to enrollment and after treatment including housing status, employment, engagement with family, and outstanding legal issues.

**Findings to Date:** We have successfully collaborated with two needle exchanges to link 100% of referred patients (n=19, 4 women, 15 men) to care at the health center. 14 of these 19 patients have come weekly for appointments, with longest participants engaged for 5 months on a weekly basis (of the remaining 5, 2 are incarcerated, 1 moved out of state for family, and 1 switched to methadone.) We have had 0 patient overdoses (and >8 overdoses among friends of participants not in the program including 7 deaths). 100% of patients had STI screening completed, serologies or initial immunizations for HAV and HBV, HCV

genotype, viral load, and fibrosis panel staging and received education on HCV natural history and transmission and harm reduction including intranasal naloxone. 1 patient had cellulitis treated who stated he would have gone to the ER for this problem prior to this program. Patients have engaged in care for other medical problems, including knee arthroscopy, breast mass evaluation, eye and dental care. CHW interventions included: getting patients IDs, securing or helping to prevent loss of current housing, free cell phones, transportation assistance, help with legal issues and court cases, and medication adherence monitoring and assistance.

**Discussions and Conclusions:** We created a sustainable model for collaboration between health centers and public health programs, with a toolkit for other CHCs to reproduce our intake and follow up of these patients. This model shows a non-traditional, open-access outpatient buprenorphine treatment model is effective in retaining patients in addiction treatment successfully without lengthy intake, counseling groups, or mandates. Many participants report negative interactions with the health care system in the past and have been appreciative of a program that treats them with dignity and respect. Participants with active injection drug use are motivated to address their hepatitis C infection and participate in evaluation and treatment. CHWs are effective at providing short, time-limited interventions including linkage to care, adherence support and assistance with housing and legal issues. Many patients have co-morbid psychiatric conditions and self-medicate with gabapentin, clonidine and benzodiazepines. Transitioning to more appropriate medications and timely access to psychiatric services has been a challenge. This collaboration of public health, medical and social services resources has allowed us to engage and treat very high risk patients and hopefully start to stem the tide of overdose deaths and the spread of hepatitis C.



## **Category: Quality Improvement / Education**

### **Empowering Internal Medicine Residents to Discuss Advance Care Planning in Primary Care Clinic**

Jessica Bender, Jennifer Russo, Irina Vovnoboy, Ryan Chippendale, Sandhya Rao,

**Needs and objectives:** Advance care planning (ACP) in primary care is increasingly important as the population ages, yet internal medicine trainees report lack of confidence and skills in leading these discussions. We conducted a needs assessment and educational intervention to improve the confidence and skills of IM interns in discussing ACP in the primary care setting.

**Setting and participants:** Boston Medical Center; Internal Medicine Interns

**Description of the program/intervention:** A voluntary needs assessment survey was conducted to assess interns' attitudes about and confidence in leading ACP discussions in the primary care setting. Based on this needs assessment, several educational interventions were developed. First, a practice improvement module was created; each intern was asked to perform a chart audit to determine their baseline practice of ACP in primary care clinic. Second, based on the results of the needs assessment survey, a one hour, small-group educational session was developed to address areas of lower confidence. After the educational sessions, participants will conduct a second chart audit to determine if their practice has changed. In addition, a post-intervention survey will be conducted to determine if interns' confidence and attitudes have changed.

**Evaluation-measures of success:** The needs assessment survey response rate was 86% (n=38). 68% had not had formal medical school training in ACP. 74% indicated that ACP in primary care is important or very important. However, 45% reported that they had not facilitated any ACP discussions with their primary care patients. Despite this, interns reported a high level of confidence in discussing advance directives, naming healthcare proxies, and facilitating ACP in the ambulatory setting. Interns reported lower confidence (able to perform with distant or close supervision) in estimating prognosis and discussing changes in care needs. The most frequently reported barriers to facilitating ACP discussions were time (87%), patients with multiple comorbidities (76%), and provider confidence (42%). The most frequently reported factors that led to high prioritization of ACP were patient age (32%), functional decline (26%) and the existence of multiple comorbidities (24%).

**Discussion/reflection/lessons learned:** This needs assessment survey indicates that participants had high levels of confidence in discussing ACP, yet they reported holding very few discussions in the primary care setting. It is possible that interns' high level of self-reported skill is due to experiences they have had in the inpatient setting, where they frequently are responsible for assisting patients in naming healthcare proxies, discussing goals of care, and leading family meetings. The interns' lower confidence in estimating prognosis in the outpatient setting likely results in an underestimation of the number of primary care patients who would benefit from ACP. Thus, the goal of the educational session was to increase interns' ability to identify patients who would benefit from APC discussions. To facilitate this, the sessions focused on improving skills in prognosticating and on sharing strategies to overcome other barriers such as time and multiple comorbidities. The aggregate results of the initial and follow-up chart audits are still pending at this time but will be used to determine if this educational intervention results in a change in practice facilitating ACP with primary care patients.

**Category: Senior Talk**

**All Work and No Play Makes Jack/Jill a Dull Boy/Girl, and Patients Unsafe?**

Sacolick, Evan

In 1984 Libby Zion was admitted to New York Hospital and unfortunately passed away within eight hours of her admission. Her death sparked an investigation of the medical residency education system that led to some major changes in both the supervision of residents and resident work hours. These events led to the ACGME duty hour restrictions that are currently present. The evidence behind the duty hour regulations is largely inconclusive because of their limited power and increase in pass offs. However, there are currently a few randomized controlled trials that compare strict duty hour restriction to a more lenient system which are currently in process.

**Category: Quality Improvement / Education**

**Reducing 30 day readmissions after acute myocardial infarction: a multidisciplinary approach to risk assessment and risk reduction**

Omar Siddiqi MD, Harpaul Sandhu MD, Deepa Gopal MD, Tamanna Singh MD, Lindsay Arnold Pharm D

**Background:** Acute myocardial infarction (AMI) all-cause 30-day readmission rates are about 20% nationwide. Higher readmission rates are associated with lower patient satisfaction, worse clinical outcomes, and reduced Medicare reimbursement rates. We sought to determine the factors that contribute to AMI readmission and to assess if a multi-faceted, bundled, pre-discharge initiative could reduce all cause 30 day readmissions after an index admission for AMI at an urban academic tertiary care center.

**Methods:** A retrospective chart review analysis was performed on all AMI patients, defined as Type I NSTEMI or STEMI, admitted to a cardiology service from May 1<sup>st</sup> 2013 to April 30<sup>th</sup> 2014 compared to historical controls from May 1<sup>st</sup> 2012 and April 30<sup>th</sup> 2013. The intervention group underwent intensive pre-discharge pharmacy counseling, social work consultation, and bedside delivery of critical medications. The control group consisted of those AMI patients discharged from a cardiology service in the year leading up to the intervention period. The primary outcome was rate of all cause 30 day readmissions. The secondary outcome was attendance at out-patient cardiology follow up within seven to ten days.

**Results:** There were four hundred and ten patients in the control group and three hundred and twenty-nine in the intervention group. The control group had 252 males (61.4%) compared to 202 in the intervention group (61.3%). The average age in the control group was 66.6 years, compared to 66.9 in the intervention group. The intervention group had a higher rate of known coronary artery disease ( $P = 0.02$ ), diabetes ( $P = 0.036$ ), hypertension ( $P = 0.04$ ), and hyperlipidemia ( $P = 0.008$ ). The rate of all cause 30 day readmission was 16.6% (68) in the control group and 13.7% (45) in the intervention group ( $p = 0.27$ ). 75% (309) of patients in the intervention group and 76% (249) in the control group followed up in a cardiology clinic within 7 days of discharge ( $P = 0.92$ ). Multivariate analysis showed a positive correlation with diabetes (OR 1.96, 95% CI 1.13-3.40), Black race (OR 2.05, 95% CI 2.0-3.50), history of frequent readmissions (OR 3.46, 95% CI 1.50-7.97) and homelessness (OR 4.22, 95% CI 1.95-9.13) with 30 day all cause AMI readmissions.

**Conclusion:** There is currently a lack of consensus regarding optimal strategies for preventing all-cause 30 day readmissions after an AMI index admission. This subject has become particularly relevant in the context of new Medicare reimbursement strategies which penalize hospitals for early readmissions. Our data suggests that an intensive, multi-faceted, bundled pre-discharge process can lead to a sustainable process to reduce all cause 30 day readmissions after an index admission for AMI.

## **Category: Quality Improvement / Education**

### **Audience response system is more effective than paper-based pre-testing to evaluate baseline resident knowledge: A prospective controlled study.**

Mayank Sardana, MBBS; Sheilah Bernard, MD, FACC

**Introduction:** Audience Response System (ARS) has previously been shown to improve the audience participation and post-test scores in small studies, although a recent systematic review failed to show its effectiveness in improving learning outcomes. We sought to prospectively assess long-term retention during ambulatory curriculum among Internal Medicine residents at Boston Medical Center with use of pre- and post-testing utilizing ARS technology.

**Methodology:** Of 19 subspecialty ambulatory blocks from July, 2013 to February, 2015, ARS (Turning Point™) was used in 4 blocks for pre-testing, which was in the form of multiple-choice questions (similar to ABIM Internal Medicine Board Exam) before relevant content was presented. In the remainder 15 blocks, paper-based pre-testing was used, whereas post-tests (same as pre-tests) were all paper-based and were given four weeks later. To get real-time assessment, no incentives or special instructions were provided after first lecture and data from first two lectures was excluded in analysis.

**Results:** On performing paired and unpaired t-test analysis of 1079 test scores, mean scores improved from pre-tests to post-tests in both formats of assessment (19% in ARS-based and 9% in paper-based; both  $p < 0.05$ ). Using paired t-testing and ANOVA, pre-test mean scores were significantly lower in ARS based group compared to paper based group (54% vs 61%;  $p < 0.05$ ), whereas post-test mean scores were not statistically different (74% vs 70%;  $p = 0.4$ ). Resident participation in pre-testing was significantly higher in ARS group compared to paper-based group (69% vs 33%;  $p < 0.001$ ).

**Conclusion:** ARS based pre-testing embedded in lecture presentation is more effective than traditional paper-based pre-testing in accurately assessing baseline resident knowledge. This leads to improved resident participation and more effective evaluation of ambulatory curriculum. Medical educators should be trained to utilize similar ARS-based assessments across all curricula in UME, GME and CME.

**Limitations:** Decreased pre-test scores in ARS based group could also be related to the subspecialties utilizing this technology or limited exposure of residents to these subspecialties in non-ambulatory settings. (Rheumatology, Nephrology and Heart Failure)

**Category: Senior Talk**

**Evolution of Myocardial Infarction: A Historical Perspective on Cardiology and its Defining Diseases**

Sharma, Prateek

“Our advances as a field of medicine are sometime difficult to appreciate from within the field, especially when it comes to Cardiology and myocardial infarction. For the lay-person there can be no more serious an event than a “heart attack,” but in medicine management of ACS have become quite routine. By examining the basis of discovery in cardiology that lay the foundation for our current understanding and treatment of MI we can appreciate not only how the general public sees medicine, but also how important collaboration and a fearless drive for discovery have been. By examining the very basis of discovery we will see some of the challenges that were overcome to lay the foundation for modern medicine and appreciate how individuals outside of medicine may currently view our abilities to diagnosis and treat these conditions. The emphasis on the historical discoveries will highlight how rapid recent breakthroughs have been and the importance of a collaborative effort, as demonstrated by evolution of MI at BMC.”

## Category: Clinical Research

### The Impact of Health Literacy on Patient-Reported Outcomes in Inflammatory Bowel Disease

Lauren Tormey, Jason Reich, Singh Arush, Yu Chen, Janice Weinberg, Francis Farraye, Michael Paasche-Orlow

**Background:** Adults with inflammatory bowel disease (IBD) engage in complex health decisions throughout the course of their lives. Health literacy (HL) can be defined as the extent to which individuals have the capacity to obtain, process and understand basic health information that is needed to make appropriate health decisions. Limited HL has been associated with worse health outcomes in several contexts; however, the role of HL for patients with IBD has not been previously examined.

**Aim:** Evaluate the impact of limited HL on the health of adults with IBD at an academic, inner city safety-net hospital.

**Methods:** A convenience sample of English-speaking adults (age > 18yrs) with IBD were recruited from the outpatient gastroenterology department. After an in-person informed consent process, interviews were conducted. HL was measured with the Newest Vital Sign (NVS), a 6-item validated HL assessment. A score of  $\leq 3$  on the NVS was defined as indicating limited HL. Medication self-efficacy (SE) was evaluated using the Medication Use and SE Scale (MUSE). Colonoscopy SE was assessed using the Highly Certain SE Scale. A pilot disease-specific knowledge questionnaire was administered. Health-related quality of life (HRQoL) was measured using the Short Inflammatory Bowel Disease Questionnaire (SIBDQ). Depression was assessed using the 4-question NIH Patient-Reported Outcomes Measurement System (PROMIS) instrument. Overall subjective health status was measured on a scale of 1 to 5. The Harvey-Bradshaw Index (HBI) and Simple Clinical Colitis Activity Index (SCCAI) were used to assess disease activity. This study is ongoing to reach target enrollment of 200. The relationship between HL level and these constructs was evaluated using the Wilcoxon rank-sum test.

**Results:** Ad interim analysis of 53 patients (36 with Crohn's disease, 17 with ulcerative colitis) enrolled into this prospective cohort study in the fall of 2014 is presented. Study participants were 22 to 84 years old and had an average age of 48.3 (SD = 17.7). About half were female (N = 28, 53%) and 35 (66%) were non-Hispanic white. Fully, 25 (47%) were college graduates, 33 (62%) were employed (part or full-time) and only 20 (38%) reported insufficient finances. Of the 53 participating subjects, 38% (N = 20) had limited HL. Limited HL was significantly associated with the outcome measures shown in table 1.

**Conclusions:** In this pilot study of adults with IBD, ad interim results reveal a high prevalence of limited HL. Limited HL was significantly associated with greater symptoms of depression, poorer overall subjective health status and lower SIBDQ scores. Interventions targeting health literacy in adults with IBD and their effects on IBD outcomes merit further study.

*Supported by a gift from Robin and Andy Davis.*

## Category: Clinical Research

### Associations of 1-Year Mortality in Systemic Light Chain AL Amyloid Heart Failure

Usman Tahir<sup>1,2</sup>, John S. Kim<sup>1,2</sup>, Lawreen Connors<sup>2</sup>, Flora Sam<sup>1,2</sup>

<sup>1</sup>Boston Medical Center; <sup>2</sup>Boston University School of Medicine

**Background:** Cardiac amyloidosis due to clonal immunoglobulin light chain (AL) is a potentially fatal disease. The median survival in AL cardiac amyloidosis (ALCMP) is <6months if untreated. However, cardiac involvement in AL amyloidosis does not always lead to clinical heart failure. The characteristics and prognosis of heart failure in patients with ALCMP have not been well characterized. We sought to determine clinical characteristics and associations of clinical markers with mortality in ALCMP with heart failure.

**Methods:** All biopsy proven ALCMP patients with Stage C heart failure presenting to the Amyloid Clinic at Boston University Medical Center from 2004-2014 were retrospectively studied. Clinical, laboratory and ECHO data were collected at initial visit to this clinic. ALCMP patients were divided into survivors and non-survivors. Clinical data was analyzed using student t test and median values were used to identify factors associated with 1-year mortality using Fischer exact formulas.

**Results:** We identified all ALCMP with heart failure who had not received autologous stem cell transplant (SCT) or immunosuppression. This cohort comprised of 165 patients. Mean age was 61.6±9.8 yrs., predominantly white (76.4%) and 60.6% were men. At 1 year, the mortality rate was a 53.3%. Mortality was associated with an older age, 64.01±9.6 vs. 58.9±9.4 yrs. (p<0.0001); higher BNP (pg/ml), 1305.4±1218.8 vs. 613.1±674.2 (p<0.0001); worse NYHA functional class, 2.94±0.57 vs. 2.37±0.51 (p<0.0001) and lower sodium(mEq/L), 138±4.2 vs. 139.2±3.0 (p=0.04). ECHO parameters associated with mortality included a lower LVEF (%), 46.6 ± 11.9 vs. 53.5 ±10.3 (p<0.0001) and lower cardiac index (L/min/m<sup>2</sup>), 1.52± 0.59 vs. 1.91± 0.64 (p=0.0003). At 1 year, LVEF <50%, BNP> 654 (pg/mL), GFR <70 (mL/min/1.73m<sup>2</sup>), CRP >4 mg/L and a history of atrial fibrillation were independently associated with mortality.

**Conclusions:** Despite novel immunosuppressive regimens mortality remains inordinately high in ALCMP with heart failure. In addition to using cardiac biomarkers, NTproBNP and troponin, which are powerful predictors of prognosis and are used to guide staging and treatment in ALCMP, we identified levels of CRP, sodium, cardiac index and atrial fibrillation as other markers associated with mortality in AL CMP heart failure. Advanced stages of heart failure defined by biomarkers and symptoms as well as objective measures of cardiac involvement on ECHO portend a poor prognosis. These markers can be used to stratify patients who might benefit from advanced amyloid therapy, while previously excluded due to their cardiac status.

## **Category: Senior Talk**

### **Mapping Health Disparities in Boston**

Katy Thompson

**Mentors:** Craig Noronha, Jessica Bender

We live in the country that spends the most on healthcare per capita, in the state that spends the most on healthcare, and in the city that spends the second most of any city on healthcare. We are in a city that, despite its numerous hospitals, community health centers, and medical schools, has vast disparities in the health of its citizens. This is illustrated across many disease conditions, when prevalence and incidence are mapped by neighborhood. The life expectancy in Back Bay is around 92 years, while in Roxbury, just over a mile away, the life expectancy is only 59 years. Universal health care in Massachusetts, by disproportionately increasing insurance coverage for minority populations, was a step in the right direction, but recent studies have shown that despite this mandate in 2006 resulting in 3% decreased mortality across the state, this decrease did not seem to specifically impact minorities. Additionally, the rate of hospitalization of minorities for conditions that are thought to be preventable with adequate access to primary care did not decrease after the universal health care was instituted. As a medical profession, we are still not proficient at consistently providing existing interventions that we know are effective at improving health. While the prior century was a century of innovative medications and technologies, the coming century should focus on how we can maximize the equitable delivery of interventions we know are effective at improving the health of diverse populations. More funding resources should be aimed at better understanding how we can improve health in this city and state for all people.



## Category: Quality Improvement / Education

### **The LEAN A3 Problem-Solving Approach is Effective in the Development and Implementation of an Early Mobilization Protocol with Associated Improved Patient Outcomes in a Medical Intensive Care Unit**

Mayanka Tickoo, Avital Rech, BSN, CCRN, Kara Schworm, MSPT, Andrea Forman, BS, RRT, Katrese Williams, Sarah Won, DPT, Karen Mattie, MS, PT, Michael Jeong, MD  
Boston Medical Center, The Pulmonary Center, BUSM

**Rationale:** Early mobilization of critically ill patients in the ICU has been shown to reduce ICU and hospital length of stay, increase functional status at hospital discharge, and reduce hospital readmission or death 1 year after discharge. Although it has widely been accepted as the standard of care for ICUs, implementation of this practice can be challenging. This challenge is particularly notable in MICUs due to the perceived limitations of mobility incurred by multiple chronic comorbidities in these patients. We embarked on a quality improvement (QI) initiative to implement a standardized approach for MICU patients which was multidisciplinary and employed the LEAN A3 Problem-Solving approach to develop a daily process of promoting early mobilization of these patients.

**Methods:** We convened a multi-disciplinary team including physicians, nurses, physical therapists, respiratory therapists and a quality analyst skilled in the LEAN A3 problem solving approach. Such an approach includes identifying the key question, describing initial and target states, establishing scope, fishbone gap, and engaging in plan, do, study, act (PDSA) cycles to allow for rapid improvement. The initial cycle was begun November 2013, with subsequent cycles through June 2014. Key metrics included performance metrics (percentage of patients assessed and mobilized, average mobilization scores targeted and achieved, number of physical therapy consults) and patient outcomes (University HealthSystem Consortium (UHC) length of stay index, mortality index, and mean ICU days). A subgroup analysis of differences in intubated and non-intubated patients was also performed. Balancing metrics including number of extubations, line displacements, hemodynamic instability were also tracked.

**Results:** PDSA cycles addressed scoring system and tracking measure improvements. Over the course of the QI project >90% assessment and mobilization attempts of ICU patients was achieved and sustained. EM was associated with a reduction in mortality index, length of stay index (see figure) and mean ICU days for the extremes of illness severity. The number of physical therapy consults doubled over this time. There was one episode of change in patient's clinical status during a mobilization attempt. The early mobilization was more vigorously implemented in non-intubated patients (average mobilization score 1.14/4) compared to intubated patients (average mobilization score 2.29/4).

**Conclusions:** The LEAN A3 problem solving method is an effective approach for developing and implementing a standardized early mobilization protocol in a MICU. Such a strategy may lead to associated reduction in relevant patient outcomes like length of stay and mortality with minimal adverse patient events.

## Category: Clinical Research

### Estrone may be more important than testosterone and estradiol for bone health and prevention of fracture in women after menopause

Gianluca Toraldo<sup>1</sup>, Thomas G. Travison<sup>2</sup>, Xiaochun Zhang<sup>2</sup>, Kerry Broe<sup>2</sup>, Shalender Bhasin<sup>3</sup>, Doug K. Kiel<sup>2</sup>, Andrea D. Coviello<sup>1</sup>

<sup>1</sup>Department of Medicine, Boston University, Boston, MA

<sup>2</sup>Institute of Aging Research, Hebrew Senior Life, Harvard Medical School, Boston, MA

<sup>3</sup>Brigham and Women's Hospital, Harvard University School of Medicine, Boston, MA

**Background:** Estradiol (E2) and testosterone (T) have been associated with bone mineral density (BMD) in post-menopausal women. T effects may be independent of estrogen or may enhance estrogen effects on bone. After-menopause, Estrone (E1) is more abundant than E2, but is considered less potent. The role of endogenous estrone (E1) in bone health is unclear.

**Objective:** To examine the associations between endogenous sex hormones T, E2, and E1 in women not using hormone replacement therapy and 1) bone mineral density (BMD), and 2) incident fracture risk.

**Methods:** BMD and fracture risk were evaluated in 829 post-menopausal women in the FHS Offspring cohort. BMD was determined by DXA in all women and by quantitative CT scan (QCT) of L3 in a subset of 304 women (total volumetric BMD, volumetric trabecular BMD, cross-sectional area). T, E2 and E1 were measured by LC/MSMS. SHBG was measured by immunofluorometric assay. Free T (FT), E2 (FE2) and E1 (FE1) were calculated using the law of mass action. Hormone values were log transformed prior to analysis to approximate the normal distribution. Associations between hormones and BMD by DXA and QCT were examined with linear regression. Hormones were categorized by quartile and association of fracture risk by hormone quartile was examined with logistic regression. Analyses were adjusted for age, BMI, physical activity, current smoking, and alcohol use. Incident fracture risk was also assessed by logistic regression in the 556 post-menopausal women without prevalent fracture at baseline.  $\alpha = 0.05$  (SASv9.1).

**Results:** Mean $\pm$ SD age was 65 $\pm$ 8 years (63 $\pm$ 8 years in of women with QCT). BMD by DXA: In fully adjusted models only logFE1 was associated with BMD of the hip ( $\beta=0.0019$ , 95%CI 0.0003-0.0034,  $p=0.02$ ) and spine ( $\beta=0.003$ , 95%CI 0.0006-0.0054,  $p=0.001$ ). BMD by QCT: In fully adjusted models, only logFE1 ( $\beta=0.0008$  g/cm<sup>3</sup>, 95%CI 0.0001-0.0014) was positively associated with total vertebral BMD but no hormones were significantly associated with trabecular BMD or vertebral cross-sectional area by qCT. Fracture Risk: One third of women (273/829, 33%) had a fracture at baseline. In adjusted models, lower E2 (Q1 vs $\div$  Q4 OR 3.0, 95%CI 1.4, 6.7) and FE2 (Q1 vs $\div$  Q4 OR 2.5, 95%CI 1.1, 5.6) were associated with prevalent fracture but E1, FE1, TT, and FT were not associated with fracture. Of the 556 women who did not have a fracture at baseline, 81 (15%) had an incident fracture over 12 years of follow up. Only lower FE1 was associated with incident fracture risk (FE1 Q1 vs $\div$  Q4 OR 12.6, 95%CI 1.8, 86.6).

**Conclusion:** Testosterone was not significantly associated with BMD or fracture risk. Estrone, the predominant estrogen in post-menopausal women, may have a role in bone health and fracture prevention in older women. As a weaker estrogen than estradiol, estrone treatment may have a role in treatment of osteoporosis with less risk of tissue exposure in the breast seen with more potent estrogen formulations.

## Category: Quality Improvement / Education

### Bedside cardiac assessment – A study to assess the efficacy of MDMF teaching method.

Verma R, Meisel JL, Cohen GM, Guarino AJ, Chen D.

**Background:** There is no universally accepted method of teaching bedside cardiology assessment to medical students. At Boston University Medical Center, two experienced clerkship directors take a multidimensional, multi-format (MDMF) approach to teaching, touching on multiple intelligences; using learning and thinking styles/preferences and cognitive scaffolding; and matching methods to objectives<sup>1</sup>; and using Heath and Heath's "SUCCES" framework to help messages "stick."<sup>2</sup> The content of the custom curriculum included relevant exam techniques and interpretation of their clinical significance (i.e., pathophysiology and impact on differential diagnosis); and a systematic approach to patient evaluation. This content was built around a six-step framework and aural mnemonics taught by Michael Gordon from the University of. In addition to aural mnemonics, the instructors used blackboards, a human demonstration, "rewind" scenario-type cases and an online heart sounds simulator.

**Objective:** To assess the efficacy of this approach to teaching bedside cardiac assessment to year 3 medical students.

**Methods:** We designed a quasi-experimental study to assess the efficacy of the 70 minute teaching seminar for 3<sup>rd</sup> year medical students at Boston University. We hypothesized that students exposed to the intervention would gain, be able to use and would retain knowledge and skills related to the intervention. Six 7-8 week blocks (~ 180 students) of 3<sup>rd</sup> year medical students rotating through their medicine clerkship were non-randomly distributed into intervention vs control groups. Students rotating through BMC medicine teams became a part of the intervention group and the student who had their rotation at other sites (West Roxbury VA, Jordon, Metro West and Roger Williams Hospitals) became a part of the control group. We developed a questionnaire based on the learning objectives of the seminar. 1<sup>st</sup> and 2<sup>nd</sup> block data were used solely to validate and optimize the questionnaire. The remaining 4 blocks of data were used to answer the study question. We administered the survey as a pre-test to all the 3<sup>rd</sup> year medical students starting their medicine clerkship at the orientation. 3<sup>rd</sup> year medical students who were at BMC received the seminar (intervention) as a part of their didactic teaching sessions. In the middle to end of their 8 weeks medicine clerkship, the same questionnaire was administered as post-tests either during their other didactic sessions or during their clerkship director meetings.

**Data collection is ongoing and we will be able to share the results when analysis is completed.**

<sup>1</sup> Meisel JL, Chen DCR. Using educational principles to create an exciting multidimensional-multiformat teaching experience. Boston University Center for Excellence and Innovation in Teaching, 3<sup>rd</sup> Annual Instructional Innovation Conference, Boston, MA. <http://www.bu.edu/ceit/files/2011/03/UPDATED-Chen-Meisel-BU-Presentation-3-25-2011-version-8.ppt>, accessed May 23, 2013.

<sup>2</sup> Heath C, Heath D. Made to stick. Why some ideas survive and others die. Copyright 2007 Random House, New York.

## Category: Clinical Research

### Open Lung Biopsy in Mechanically Ventilated Patients with Suspected Acute Respiratory Distress Syndrome: a Meta Analysis.

Wong, Alexandra; Walkey, Allan

**Background:** Open lung biopsy may be performed to clarify diagnosis and guide therapy in patients with suspected acute respiratory distress syndrome (ARDS). However, most data regarding the yield of lung biopsy in mechanically ventilated patients with suspected ARDS comes from single center case series. We sought to describe the distribution of diagnoses, assess complications, and determine changes in therapy following lung biopsy in mechanically ventilated patients with bilateral infiltrates of unclear etiology.

**Methods:** We systematically searched Medline for case series of lung biopsies in patients with suspected acute lung injury, ARDS, or respiratory failure with lung infiltrates of unclear etiology. We excluded studies that included only pediatric or immunocompromised patients.

**Results:** We identified 14 case series spanning years 1976-2013 that included a total of 527 patients. Average age of patients was  $51.4 \pm 5.2$  years, 52% were male, with an average of  $7.6 \pm 4.2$  days on mechanical ventilation prior to lung biopsy. Biopsy yielded 554 histopathological results (27 patients with 2 diagnoses). The most common diagnoses following lung biopsy were diffuse alveolar damage (n=86, 15.5%), viral pneumonia (n=85, 15.3%), interstitial fibrosis (n=76, 13.7%), interstitial pneumonitis (n=43, 7.8%), bacterial pneumonia (n=28, 5.1%), malignancy (n=25, 4.5%), bronchiolitis obliterans organizing pneumonia (n=24, 4.3%), and fungal infection (n=14, 2.5%) (Figure). Therapy was changed following lung biopsy in 393/527 (74.5%) patients. Procedure-related complications occurred in 26.4% of patients. The majority of these complications were related to persistent post-operative air leaks, and included air leak not otherwise specified, pneumothorax, bronchopleural fistula, and subcutaneous emphysema (n=99, 18.8%). Other complications included intraoperative hypotension requiring intervention (n=9, 1.7%), hemothorax (n=9, 1.7%), progressive hypoxemia (n=8, 1.5%), and acute kidney injury (n=7, 1.3%). Other complications (blood loss, empyema, wound infection, death) occurred in fewer than 2% of patients. In 12/14 case series reporting hospital or 28-day mortality after lung biopsy, patient mortality was 60%.

**Conclusions:** Among mechanically ventilated patients with respiratory failure and bilateral infiltrates of unclear etiology, lung biopsy yielded a wide range of diagnoses and appeared to change therapy in most patients. Bronchopleural fistulae were common complications. In patients with suspected ARDS who fail to improve with conventional treatment of the suspected underlying cause, open lung biopsy may be useful to determine specific diagnoses and tailor treatment. Mortality in patients undergoing lung biopsy was relatively high; thus, whether risks of lung biopsy outweigh benefits in critically ill patients is unclear.

## Category: Clinical Research

### Efficacy of Bortezomib in the Treatment of Plasma Cell Leukemia

Yameen, Hassan

**Introduction and Background:** Plasma cell leukemia (PCL) is defined as absolute plasma cell count exceeding 2000/microL or 20% of the peripheral WBC count. Presence of plasma cells in peripheral blood distinguishes PCL from other plasma cell neoplasms. PCL is extremely aggressive with rapid progression and dismal prognosis. The 2 types are Primary PCL (disease arises de novo), and Secondary PCL (disease arises as a natural progression of pre-existing multiple myeloma.) Many genetic abnormalities seen in PCL is also present in high risk multiple myeloma (MM). The diagnostic work up is the same as that for MM. There is a gaping lack of knowledge regarding the most effective treatment for PCL. Recommendations are primarily based upon extrapolation of data from studies done with MM patients. Research shows that newer agents like bortezomib is very effective in patients with high risk multiple myeloma as defined by genetic abnormalities. It is reasonable to assume that bortezomib will be effective in PCL too as it shares many common genetic abnormalities as high risk MM.

**Methods:** A systematic review of all the available scientific literature about the use of Bortezomib or Bortezomib based regimens (BBR) for the treatment of plasma cell leukemia was conducted. Medline (PubMed), Cochrane Library, and NIH's ClinicalTrials.gov databases were searched for observation studies as well as clinical trials using controlled vocabularies (MeSH terms, and key word searching for 'Plasma Cell Leukemia' and 'Bortezomib'.

**Results:** A search on PubMed brought up 87 results, none of which were randomized clinical trials. A case series of 29 patients showed a 79% response rate with significant improvement in survival. A multicenter retrospective cohort study with 128 patients showed improved outcomes. A case control study with 42 patients with BBR vs conventional therapy showed response rates 69% vs. 30.8% ( $P = 0.04$ ), and median overall survival 13 vs. 2 months ( $P < 0.007$ ). A review of 25 patients with bortezomib vs. non-bortezomib therapy showed a median survival of 28 months vs. 4 months. A search on NIH's ClinicalTrials.gov brought up a few single arm phase I and phase II studies ongoing with bortezomib in patients with plasma cell leukemia. A search for studies in the Cochrane Library brought up 4 results none of which were relevant.

**Conclusions:** There is lack of data, evidence, and knowledge with regards to treatment of PCL, both for induction chemotherapy as well as post-stem cell transplant maintenance therapy. There are no randomized control trials (RCTs) in the literature. Current guidelines are primarily based upon data from case reports, small observational studies, and extrapolation of data from MM trials. Many induction chemotherapy regimens for PCL are bortezomib-based as a result. Current approach is to follow the induction chemotherapy with autologous stem cell transplantation similar to the treatment of MM. More studies focusing on PCL, especially RCTs, will be critical in our quest for finding evidence-based treatments for this rare and aggressive malignancy.