



Internal Medicine Residency Program

Boston University Medical Center

**Senior Resident Academic
Day Friday, May 31, 2013**

Handbook of Abstracts

BOSTON UNIVERSITY INTERNAL MEDICINE RESIDENCY PROGRAM

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When Eosinophils Go Wild

Anitha Bhat MD

Introduction: Hypereosinophilic syndrome is collection of disorders which can present with a variety of different signs/symptoms. The heterogeneity of clinical manifestations and the etiologies leading to this syndrome pose challenges to the diagnosis of this condition.

Case Description: A 37 year old Guatemalan male with no known past medical history presented to the hospital with a 3 week history of fatigue, myalgias, and fevers. He had been evaluated in the emergency room 4 days prior to presentation for fevers/shortness of breath; at that time, chest x-ray showed a left lower lobe opacity and CT angiogram showed a left sided pleural effusion with compressive atelectasis. He was sent home with a course of azithromycin. On the second presentation to the hospital, his admission exam was notable for an oxygen saturation of 95% on room air, and decreased breath sounds at the left lung base. His admission labs were notable for white count of 115,000 cells/ul with an absolute eosinophil count of 2600 cells/ul (no documented priors). The patient was initially started on ceftriaxone for community acquired pneumonia. Preliminary workup for his eosinophilia, including microbial cultures was not revealing. Thoracentesis of the left pleural effusion yielded 750 ccs of eosinophil rich exudate. Over the course of his hospital stay the patient's clinical status declined; he developed cognitive impairments in orientation and memory as well as a slight left pronator drift, ataxia, and episodic abdominal pain. He had an MRI of his brain performed, which showed findings suggestive of recent small multiple infarcts distributed in both the cerebral and cerebellar hemispheres. A cardiac echogram showed a 1x1 cm pedunculated mass in the left atrium. A CT abdomen pelvis was performed given complaints of abdominal pain, and was significant for 75% splenic infarction on CT. He was started on anticoagulation and IV steroids. His eosinophil count decreased dramatically from 3600 to 200, and the patient did not have further progression of his symptoms. Hypercoagulable workup was negative, and a follow-up TEE showed resolution of the atrial mass. He was discharged from the hospital with a tentative diagnosis of hypereosinophilic syndrome.

Discussion: Hypereosinophilic syndrome is a large collection of disorders, which are characterized by the as the presence of hypereosinophilia (eosinophil count > 1500 cells/ul or tissue hypereosinophilia) with eosinophil-mediated organ damage/dysfunction. Diagnosis can be challenging, and can range from being asymptomatic to having various combinations of skin, CNS, cardiac, pulmonary, and GI symptoms as well as thromboembolic disease. In addition, there are significant similarities in the clinical manifestations (and treatment) of hypereosinophilic syndrome and Churg-Strauss disease. In patients presenting with hypereosinophilia, diagnosis is directed towards excluding secondary causes of hypereosinophilia, identifying eosinophil-mediated end-organ damage, and possibly performing hematologic/genetic evaluation to identify a myeloproliferative cause for the hypereosinophilia.

Pulmonary Hypertension: An Appropriate Diagnostic Workup

Poushali Bhattacharjee MD, Boston Medical Center, Boston, MA, Anand Kartha MD, VA Medical Center, West Roxbury, MA

Pulmonary hypertension is a near-fatal disorder when not treated, and can often be mitigated if the appropriate underlying etiology is identified. As such, when pulmonary hypertension is suspected, a thorough diagnostic workup is indicated as it can significantly alter the course of the disease as well as patient's morbidity and mortality.

A 66 year old male with history of obstructive sleep apnea on CPAP, mild COPD and atrial fibrillation on coumadin presented with progressive dyspnea on exertion and severe day-time and night-time hypoxia. The patient stated that although he had lost a significant amount of weight after a stroke, he had recently gained it all back. He has a one year history of dyspnea on exertion, that had gotten particularly worse over the past several months. He denied any orthopnea or PND, but did report progressive lower extremity edema and increasing abdominal girth. He had been following in pulmonary clinic, where he had most recently undergone overnight oximetry that revealed the patient spent 99.3% of the study at less than 90% oxygen saturation and 60.3% of the study at less than 80% oxygen saturation. At that point, he was directly admitted for expedited workup of his severe hypoxia. On arrival to the floor, the patient appeared comfortable but was visibly short of breath. His vitals were significant for an oxygen saturation of 90% on 4L of oxygen via nasal cannula. His face was plethoric and he had a large neck. His cardiac exam revealed an irregularly irregular rhythm without any murmurs and jugular venous distention could not be appreciated due to his body habitus. A right ventricular heave was not palpated. His lungs had diffuse, faint expiratory wheezes but no crackles. No shifting dullness was appreciated on his abdominal exam. He had 3+ lower extremity edema bilaterally to his mid-thigh. Because he showed clinical signs of right heart failure, he was started on an aggressive diuretic regimen with lasix. He then underwent extensive testing to rule out secondary causes of pulmonary hypertension. The patient underwent a TTE that revealed preserved left ventricular function but severe right ventricle and right atrial enlargement with an estimated pulmonary artery systolic pressure of 58mmHg. A CTPA was performed that did not show any signs of interstitial lung disease or thromboembolic disease. HIV was negative and ANA weakly positive. During that admission, he also underwent right heart catheterization which revealed elevated right and left sided filling pressures and moderate to severe pulmonary hypertension. His symptoms improved dramatically with diuresis. He was discharged with close follow up in pulmonary clinic at which time further studies were pursued both to rule out shunt physiology (with bubble study) and to ensure no other autoimmune cause was contributing to his presentation (with RF and ANCA). These tests had a negative result, so his pulmonary hypertension was thought to be due primarily to diastolic dysfunction as a result of COPD, OSA, and obesity hypoventilation syndrome with a minimal component of primary pulmonary hypertension. To ensure that there were no other areas of intervention to improve his hypoxia, repeat PFTs were performed that revealed worsening COPD so his medication regimen was further optimized. Another sleep study showed resolution of nocturnal hypoxia, and repeat TTE showed a decrease in pulmonary artery systolic pressure from 45 to 32; however further workup is pending to see if he is a candidate for vasodilator therapy. He was then referred to cardiology for management of his diuretic regimen.

This case illustrates that there are a variety of unrelated diseases that can result in pulmonary hypertension, and that correct identification via a thorough and extensive workup can directly alter the clinical course and management of the disease.

Paternalism and Autonomy of Adult Patients in the Clinical Setting

Author: Cohn, H. Matthew

Abstract: My interest in medical paternalism is routed, like most of our clinical interests, in a patient encounter. As a newly promoted junior resident in internal medicine, I saw a patient at the Ambulatory Diagnostic and Treatment Center (ADTC) clinic of the Jamaica Plain VA hospital. The patient was an elderly man, hard of hearing, recently discharged from the West Roxbury VA Hospital with a diagnosis of metastatic cancer. He was accompanied by his son who asked me in a soft but audible voice, not to share the diagnosis with the patient. Having believed I only knew a world of patient autonomy, I was both disturbed and intrigued by this practice of information withholding. Following this vignette, I will begin my talk with a definition of terms and provide a history and evolution of the doctor-patient interaction with focus on paternalism and the fruition to patient autonomy via technology-oriented medicine and the practice of informed consent. I will then discuss clinical situations where patient autonomy is not always appropriate, as in the cases of the psychiatrically incompetent, intellectually disabled, and patients with dementia. I will then expand this concept to issues of end of life care, specifically its relationship with medical futility and the overall consequences of resource allocation. Continuing with the impact of public health, I will briefly discuss active paternalistic issues of antibiotic treatment, growing resistance and the need of physicians to sometimes respect the autonomy rights of the public over the individual. The discussion will then shift to well-accepted prohibitions that are potentially overly paternalistic, as in the ban of organ sales, physician-assisted suicide, and euthanasia. A brief discussion of *Cruzan v. Director, Missouri Dept. Of Health* will underscore this concept. The discussion's conclusion will begin with a summation of the highlighted points, personal thoughts and a finish to the aforementioned vignette. My talk will end with a stirring quotation in defense of medical paternalism taken from an article published posthumously by *The New England Journal of Medicine* titled "Arrogance" based on the George W. Gay Lecture delivered by Dr. Franz Ingelfinger on May 5, 1977. Other resources will include *Bioethics*, *Hastings Center Report*, *American Journal of Law & Medicine*, *Annals of Internal Medicine*, amongst other periodicals. The eminent *Principles of Biomedical Ethics* by Tom Beauchamp will also be cited.

Challenges in the Delivery of Quality Breast Cancer Treatment at an Urban Safety Net Hospital: Initiation of Adjuvant Hormone Therapy

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Background: Breast cancer treatment disparities in minority and low income populations are well documented, however the underlying reasons remain poorly understood. The purpose of this study is to identify patient characteristics and patient level barriers to receipt of quality breast cancer care, specifically addressing compliance with the National Quality Forum (NQF) quality metric for adjuvant hormone therapy (HT) (administration of HT within 365 days of diagnosis in eligible patients) at an urban safety net hospital.

Methods: This retrospective observational study included women diagnosed with non-metastatic, T1c or greater, Estrogen and/or Progesterone Receptor positive breast cancer from 2006-2008. Data sources included the hospital cancer registry and electronic medical record chart abstraction. Bivariate analysis compared characteristics of compliant to non-compliant patients. Descriptive analysis assessed reasons for delayed compliance (HT at >365 days) and never compliance (no HT after 4 years follow up).

Results: There were 113 eligible patients. The majority were racial/ethnic minority (56%), Stage II (54%), unmarried (60%), and had public or no insurance (72%). Overall, 64% were compliant and 36% were non-compliant. Of the non-compliant, 78% had delayed compliance and 22% were never compliant for up to 4 years of follow up. Non-compliant patients were significantly more likely to be Black, Hispanic, foreign-born, and stage III at diagnosis. Ten non-exclusive reasons for delayed compliance were identified, ranging from treatment-related factors to social factors. 56% of patients had more than one reason contributing to their non-compliant status.

Conclusion: Reasons for non-compliance with the NQF quality metric for HT are complex in this underserved, diverse population. Urgent interventions to reduce the pervasive disparities in quality breast cancer treatment should take into account issues relevant to immigrant and indigent populations.

Identifying the Risks of Anticoagulation in Patients with Substance Abuse

Efird LM, Miller DR, Ash AS, Berlowitz DR, Ozonoff A, Zhao S, Reisman JI, Jasuja GK, Rose AJ. "Identifying the Risks of Anticoagulation in Patients with Substance Abuse." *J Gen Intern Med*: In Press.

BACKGROUND: Warfarin is effective in preventing thromboembolic events, but concerns exist regarding its use in patients with substance abuse.

OBJECTIVE: Identify which patients with substance abuse who receive warfarin are at risk for poor outcomes.

DESIGN: Retrospective cohort study. Diagnostic codes, lab values, and other factors were examined to identify risk of adverse outcomes.

PATIENTS: Veterans Affairs Study to Improve Anticoagulation (VARIA) database of 103,897 patients receiving warfarin across 100 sites.

MAIN MEASURES: Outcomes included percent time in therapeutic range (TTR), a measure of anticoagulation control, and major hemorrhagic events by ICD-9 codes.

RESULTS: Nonusers had a higher mean TTR (62 %) than those abusing alcohol (53 %), drugs (50 %), or both (44 %, $p < 0.001$). Among alcohol abusers, an increasing ratio of the serum hepatic transaminases aspartate aminotransferase/alanine aminotransferase (AST:ALT) correlated with inferior anticoagulation control; normal AST:ALT ≤ 1.5 predicted relatively modest decline in TTR (54 %, $p < 0.001$), while elevated ratios (AST:ALT 1.50–2.0 and > 2.0) predicted progressively poorer anticoagulation control (49 % and 44 %, $p < 0.001$ compared to nonusers). Age-adjusted hazard ratio for major hemorrhage was 1.93 in drug and 1.37 in alcohol abuse ($p < 0.001$ compared to nonusers), and remained significant after also controlling for anticoagulation control and other bleeding risk factors (1.69 $p < 0.001$ and 1.22 $p = 0.003$). Among alcohol abusers, elevated AST/ALT > 2.0 corresponded to more than three times the hemorrhages (HR 3.02, $p < 0.001$ compared to nonusers), while a normal ratio AST/ALT ≤ 1.5 predicted a rate similar to nonusers (HR 1.19, $p < 0.05$).

CONCLUSIONS: Anticoagulation control is particularly poor in patients with substance abuse. Major hemorrhages are more common in both alcohol and drug users. Among alcohol abusers, the ratio of AST/ALT holds promise for identifying those at highest risk for adverse events.

The relationship between COPD-associated gene expression in the proximal bronchial airway and the small airway epithelium

Florido R, Hijazi K, Campbell J, Liu G, Xiao J, Zhang X, Alekseyev YO, Sin D, McWilliams A, Sebastiani P, O'Connor GT, Lam S, Spira A, Lenburg ME, Steiling K

Introduction: Whole genome expression profiling of the cytologically normal bronchial airway is a powerful method that has been used to characterize a field of injury in smokers, and develop a biomarker with high diagnostic accuracy for the evaluation of patients with suspected lung cancer. In this study, we sought to extend this field of injury concept to the study of COPD using microarray profiling of the airway epithelium collected during bronchoscopy (n=238). To determine whether the COPD-associated gene expression changes in the more proximal bronchial airway were similarly changed in the small airway epithelium (10-12th generation bronchi), I compared the bronchial airway COPD signature to a previously published small airway epithelium COPD dataset.

Methods: Raw data from a previously published study profiling the 10th generation airway epithelium of subjects with and without COPD was obtained from the Gene Expression Omnibus (GEO). Data was normalized using the RMA algorithm and Entrez Gene CDF v11.0.1 in the R statistical environment. A t-test was used to compare gene expression changes in the small airways of subjects with GOLD Stage 1-2 COPD (n=4) versus smokers with normal lung function (n=12). These results were compared to the 98-gene bronchial airway signature of COPD identified in our larger cohort of 238 subjects using Gene Set Enrichment Analysis (GSEA).

Results: Using Principle Component Analysis (PCA) and Relative Log Expression (RLE) graphs, we determined that the samples in the small airway were of adequate quality for further analysis. Genes were ranked according to the t-statistic comparing small airway gene expression from subjects with and without COPD. Using GSEA, we identified that genes increased in the COPD bronchial airway signature were similarly increased in the small airway epithelium of subjects with COPD, and that genes decreased in the COPD signature were similarly decreased in the independent dataset (GSEA FDR < 0.05).

Conclusions: These findings show a consistent gene expression changes in the more proximal bronchial airway and the more distal 10-12th generation small airway epithelium. These data suggest a COPD-associated airway field of injury that can be sampled via bronchoscopy, and might serve as a relatively accessible tissue in which to measure biomarkers of COPD.

Eligibility and Enrollment Characteristics of Screened Cancer Clinical Trial Patients at an Urban Safety-Net Institution

Julie Fu MD, Naomi Ko MD, MPH, Tracy Battaglia MD, MPH, Sarah Caron

Enrollment rates onto cancer clinical trials are historically low (<2 to 11%) and reflect a small subset of the population. Can we truly generalize cancer treatment and research to the wider general population? There exists a need to increase enrollment with a focus on recruitment of a diverse, underrepresented patient population. Our goal was to understand and examine whether socio-demographic factors affect the eligibility and enrollment into cancer clinical trials at Boston Medical Center.

We looked at 847 cancer clinical trial screening notes in the year 2012 through the electronic medical record. We found that a diverse patient population was screened for eligibility, including 61% female, 56% non-White, 76% public/no health insurance. Among the screenings conducted, 18% (150 out of 847) were deemed eligible for enrollment onto a clinical trial. There were no socio-demographic differences between those eligible v. ineligible for a clinical trial. Among eligible patients, 41% (61/150) enrolled. Enrolled patients reflected our diverse patient population: 48% non-white, 66% public insurance or uninsured, 31% non-USA born, 54% high school grad or less. With regard to socio-demographic characteristics among eligible patients, a significantly higher percentage of more educated patients ($p = 0.04$) enrolled into trials.

Our high enrollment rate compared to nationwide was encouraging (41% v. <2 to 11%). Eligibility for open clinical trials at our institution was not affected by socio-demographic status, and enrollment reflected our diverse patient population. We demonstrate an ability to enroll a diverse population when open, available trials exist. This may be attributed to staff experienced in working with minorities and the underserved. As the city of Boston's safety net institution, our history has been to care for those who have fewer resources and support. Since educational level is a predictor for enrollment, there needs to be ongoing efforts to raise awareness about the benefits of participation in cancer research among those less educated and the wider community at large.

Importance of URM Representation in Medicine

Tiffany Groover, MD, MPH

Between 1978 and 2008, 75% of all medical school graduates practicing medicine were White, while Blacks or African Americans, American Indians/Alaska Natives and Hispanics or Latinos comprised a combined 12.3% of the U.S. physician workforce.

It is highly recognized that within the health professions, diversity is an essential component for promoting excellence in medical education and accessible quality health care. Research indicates that physicians from racial and ethnic minority backgrounds themselves are more likely to treat racial and ethnic minority patients, and are more likely to practice in typically underserved communities.

The Department of Health and Human Services Secretary's 1985 report estimated that thousands of excess deaths in these underserved communities were largely attributable to cancer, cardiovascular disease, diabetes, infant mortality, substance abuse, and violence. Even today, the overall health status of minorities is worse than that of whites, despite increases in both the number of physicians nationally and national health expenditures.

The rapidly changing demographic composition of the U.S. population compels a reevaluation of who will be the physician of the future, and how that physician's background and sociocultural experiences will prepare him or her for understanding each patient's needs.

When physician and patient differ with respect to race, ethnicity, language, religion and values, ensuring fair, equitable, and culturally sensitive care is more challenging. Speaking to the importance of recruiting a more diverse health professions workforce as being key to eliminating health care disparities.

The Effect of Functional Mitral Regurgitation on Prognosis in Patients with Advanced Cardiomyopathy

Mowakeaa, Samer; Grossman, Jason R; Dwivedi, Aeshita; and Aragam, Jayashri

Introduction: Patients with advanced cardiomyopathy (CMP) often develop significant mitral regurgitation despite structurally normal mitral leaflets, known as functional mitral regurgitation (FMR). Clinical and echocardiographic correlates of FMR are not well defined and the prognostic impact of FMR in patients with advanced CMP is controversial.

Methods: The medical records of 487 consecutive patients (age 69 ± 11 yr, 98% men) with left ventricular ejection fraction (LVEF) $\leq 35\%$ who underwent a transthoracic echocardiogram at a single Veterans Affairs medical center in 2009 and 2010 were reviewed. Patients with mitral leaflet pathology or significant aortic valve disease were excluded. The remaining 370 patients were categorized into three groups based on the American Society of Echocardiography guidelines for quantification of mitral regurgitation: 1) No FMR, 2) Mild FMR, 3) More than mild FMR. The following information was collected: patient demographics and co-morbidities, echocardiographic findings, and outcomes data including all-cause mortality and hospitalizations for heart failure (HF), myocardial infarction or stroke.

Results: When compared to patients in group 1, those in groups 2 and 3 were more likely to be older ($p=0.0001$), have a greater body surface area ($p=0.0003$), atrial fibrillation ($p=0.018$), a higher New York Heart Association Class ($p=0.001$) and higher creatinine levels ($p=0.001$). Echocardiographically, these patients were more likely to have greater left ventricular end-diastolic and end-systolic dimensions ($p=0.04$ and $p=0.005$, respectively), greater left atrial size ($p=0.003$), and a lower LVEF ($p=0.0001$). They also had higher pulmonary arterial systolic pressure ($p=0.0001$), and more severe tricuspid regurgitation ($p=0.001$). Unadjusted univariate Cox Model analysis showed that presence of either mild or more than mild FMR was associated with a higher risk of death from any cause [Hazards ratio (HR): 1.8, $p=0.02$ for Group 2 vs. Group 1; HR: 2.6, $p=0.001$ for Group 3 vs. Group 1] and hospitalization for HF (HR: 2.5, $p=0.002$ for Group 2 vs. Group 1; HR: 3.9, $p=0.001$ for Group 3 vs. Group 1). There was no increase in the risk of myocardial infarction or stroke in patients with FMR. After adjustment in a multivariable Cox Model, the significantly increased risk of hospitalization for HF and death from any cause persisted for group 3 (HR: 1.8, $p=0.02$).

Conclusion: In patients with advanced CMP, presence of more than mild FMR is associated with an increased risk of death from any cause and hospitalization for HF.

A Rare Presentation of Disseminated Intravascular Coagulation: A Case Report

Tina Gupta, MD, Winnie Suen, MD Department of Geriatrics, Boston Medical Center, Boston, MA

Authors: Gupta, T; Kim, E; Han, B

Introduction: Chronic DIC is a coagulation disorder where the hemostatic balance is disturbed by an excessive stimulation of normal coagulation pathway. A large (>7cm diameter) thoracoabdominal or abdominal aneurysm/dissection is known to be a rare cause for chronic DIC. Most case reports demonstrate that surgical repair of the aneurysm is the treatment of choice for this particular condition. For non-surgical candidates, different modes of heparin therapy have been successful in treating this condition in case reports. We present a case of chronic DIC in the setting of a large thoracoabdominal aneurysm, an extremely rare cause of this bleeding diathesis.

Case Description: A 70-year old Haitian-American male with a past medical history significant for hypertension and thoracoabdominal aneurysm (TAA) presented with recurrent buttock pain and severe anemia.

Physical exam was notable for diffusely tender bilateral thighs with entirely normal cardiac, pulmonary, and neurological exams. Initial workup revealed Computed tomography (CT) scans (see images) confirmed bilateral gluteal hematomas and known 7.3 cm TAA, stable from its initial presentation in 2000. Over the past year, he had presented similarly every two to three months with spontaneous hematomas and significant anemia. Labwork was significant for decreased platelets (84), elevated d-dimer (>30) and low to normal fibrinogen level (194). These findings, along with the clinical history of recurrent spontaneous bleeds, were suggestive of Chronic DIC, possibly triggered by activated endothelium of the patient's concurrent TAA.

Medical Management and Outcome: Surgical correction of the aneurysm is the standard treatment for this condition. However, considering the significant pre-operative risk in this deconditioned patient, surgery was deferred and medical management initiated with a heparin drip. Within days, there was a recovery of platelet numbers (278) and elevation in fibrinogen level (422). The patient continued with daily heparin injections on discharge until three weeks later, when he presented to the hospital with altered mental status, sudden onset emesis and headache. A CT Head revealed extensive intracerebral hemorrhage. His clinical condition deteriorated despite aggressive critical care, and he passed away two days later.

Discussion: Chronic DIC, a known complication of thoracoabdominal aneurysm/dissection, has a higher incidence than it was previously reported. With a high prevalence of long standing hypertension, TAA is often discovered in an elderly population. When patients with a known aneurysm presents with severe anemia or easy bruising, they should be checked for coagulation studies. Early recognition of this condition is essential to an appropriate treatment and cure. Delay in diagnosis may result in significant morbidity and mortality.

BMC INPATIENT DIABETES REPOSITORY

Elizabeth Herman, Marie E. McDonnell, Linda Rosen, Clara Chen, Christine Chaisson, Sara M. Alexanian, Devin Steenkamp

Objective: While the prevalence of hyperglycemia in hospitalized patients is >50% and 33% of BMC inpatients have documented diabetes, there are large gaps in clinical outcomes research in this population. We created a data repository of all adult inpatients at BMC who have had a glucose point of care test performed since 2002. It was IRB approved in June, 2012. **Methods:** The repository contains data from 2002-present and is updated quarterly. The dataset contains approximately 200 variables including glucose values, BMI, demographics, language and education level, key lab values, length of stay, medications, primary and secondary diagnoses, and automatically calculated Charleson co-morbidity index. **Outcomes:** The repository includes data from approximately 80,000 visits from 40,000 unique patients. Diabetes prevalence was based on three criteria: discharge ICD-9/10 codes, A1c >6.4, or diabetes medications prior to admission. Approximately 20,000 patients, or 50%, have Diabetes. **Conclusions:** The BMC Inpatient Diabetes Repository is an IRB-approved rich database managed by the Data Coordinating Center that can be used by BMC providers to assess quality and safety outcomes in inpatient population. In addition, it will be used to expand general knowledge by answering important research questions, or providing preliminary support for prospective research.

Early Public Health in Boston – From 1630 to the Advent of the Boston Public Health Commission

Jeffrey Jenks, MD

Public health in colonial Boston is a fascinating historical ride. Its history includes epidemic disease outbreaks, famous historical figures, revolutionary war with a capital “R”, and even murderous plots and the jailing of one of Boston's most famous physicians!

We start off with a brief look at some of the early public health challenges in colonial America, including the constant threat of infectious diseases such as influenza and tuberculosis. The most early public health efforts, which were minimal at best, concentrated on improved sanitation, as the belief at the time was that disease was spread by “evil smells” and “bad air”, a belief known as miasma.

Public health started to blossom around the threat of epidemic infectious diseases, such as yellow fever, which threatened Philadelphia and Baltimore in the 1660s. Boston was spared largely through the quarantine of ships carrying yellow fever from the Caribbean. A smallpox epidemic threatened Boston in the 1720s, prompting a local minister and physician to adopt a controversial practice of inoculating healthy people with the smallpox virus.

Smallpox again threatened Boston in 1775, jeopardizing the very success of the impending Revolutionary War. Boston was placed under quarantine, and there was rumor that a British General was even deliberately infecting displaced Bostonians with smallpox. Inoculation was again attempted to stem the spreading threat of smallpox epidemic.

By the late 1700s sanitation and mortality had improved in Boston, but yellow fever again threatened Boston. At the behest of the Commonwealth of Massachusetts a Board of Health in Boston was established, with Paul Revere as its first President. Early public health efforts again targeted improving general sanitation, with the hopes of stemming an impending yellow fever epidemic.

These early public health efforts led to the establishment of the Boston Board of Health, and eventually Boston City Hospital and the Boston Public Health Commission as we know it today. Boston didn't become a world-class healthcare center overnight...it's foundation lies partially in early efforts towards improved public health.

A Simplified Post-Discharge Telephone Intervention To Reduce Hospital Readmission for Patients with Cardiovascular Disease

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Background: Readmission rates are high for patients with cardiovascular disease, particularly heart failure (HF) and acute coronary syndrome (ACS). Telephone calls by clinical staff have had mixed effects. We aim to evaluate the degree of implementation and the effect of a quality improvement initiative using a simplified post-discharge phone call by administrative assistants.

Methods: Clinical data was retrospectively reviewed at a single urban public hospital. From January through October 2012 all patient discharged home from inpatient cardiology services (intervention group, n=1034 discharges) were identified. Within 7 days, administrative assistants contacted patients via telephone and queried regarding (1) medication compliance, (2) awareness of follow-up appointments and (3) if clinician contact is requested. Outcome events were defined as readmissions (for any cause) within 30 days to the same hospital and are reported as patients experiencing readmission, and total readmissions. A comparison group of all patients discharged home from inpatient cardiology services from January through October 2010 (n=746) were selected as controls (no phone calls). Categorical data were compared in a univariate fashion using the Chi Square test. Statistical significance is defined as $p < .05$.

Results: Of the 1034 discharge events in the intervention group, 620 (60.0%) had phone calls attempted. Of those, 419 (67.6%) were directly contacted. Patients were statistically significantly different with respect to language, ethnicity and insurance status. Of the patients called, 48 (7.7%) reported medication abnormalities, 13 (2.1%) did not understand their follow-up and 38 (6.1%) had a question for a clinician. The rates of patients experiencing events was not statistically different (132 [17.7%] vs. 156 [15.1%], OR 0.85, $p = .14$). Total readmissions were significantly reduced (157 [21.0%] vs. 179 [17.3%], OR 0.82, $p = .047$). Pre-specified subgroups of ACS and HF patients showed a trend towards decreased readmissions but were not statistically significant. Given patient population, there may be selection bias against poorer patients with decreased understanding of disease process, hospitalization, and medications who may have benefited more from phone calls.

Conclusion: A simplified post-discharge telephone call strategy is associated with a trend towards reduced hospital readmissions for cardiology patients. Further refinements are needed to improve program implementation.

Hypothyroidism is Not Associated with Increased Risk of Atrial Fibrillation:

The Framingham Heart Study

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Background: The association between hyperthyroidism and risk of atrial fibrillation (AF) is well described. In contrast, whether hypothyroidism results in increased risk of AF remains unclear. Hypothyroidism is associated with cardiovascular risk factors, subclinical and overt cardiovascular disease, all of which predispose to AF. We investigated the relation between hypothyroidism and the 10-year risk of AF in a community-based cohort.

Methods: We examined 6,653 Framingham Heart Study (FHS) participants. Participants were excluded for missing thyroid stimulating hormone (TSH), TSH <0.5mU/L (hyperthyroid), or prevalent AF. TSH was stratified as <5.0, 5.0-10.0, 10.0-20.0, ≥20.0 and by quartiles. We performed multivariable-adjusted Cox proportional hazards analysis.

Results: Following exclusions, 5,106 participants (52% women, mean age 57±12) were included in the analysis. During the 10-year follow-up, we observed 280 cases of incident AF. We determined that the association between a 1-standard deviation (SD) increase in TSH and AF did not reach statistical significance (Hazard Ratio [HR]: 0.99, 95% confidence interval [CI]: 0.885-1.11, p=0.83). Using TSH<5.0 as a referent, we found no significant association in age- and sex-adjusted analysis between hypothyroidism and 10-year AF risk employing TSH 5-10.0 (HR: 1.44, 95% CI: 0.89-2.33, p=0.14), 10-20 (HR: 0.61, 95% CI: 0.23-1.65, p=0.33) or ≥20.0 (HR: 1.02, 95% CI: 0.32-3.19, p=0.98). Furthermore, comparing the highest (TSH>2.5) to the lowest (TSH<1.3) quartiles of TSH in our cohort, the association between hypothyroidism and 10-year risk of AF was also not significant (HR: 1.25, 95% CI: 0.91-1.73, p=0.17). Excluding participants on replacement (n=323) did not alter these findings. A post-hoc power analysis identified our study would have required HR 1.26 per 1-SD increase in TSH to achieve 80% power.

Conclusion; In our community-based study, we did not identify a significant association between hypothyroidism and 10-year risk of incident AF. A study with a larger number of events may improve power to examine the relation of hypothyroidism to AF.

Use of treatment contract and urine drug testing in patients receiving chronic opioid therapy at BMC primary care clinics

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Background: Use of treatment contract and urine drug testing is widely recommended in chronic opioid therapy to ensure adherence to therapy and to monitor for misuse. Early refills of the opioid medication may indicate potential misuse. In this project, we sought to validate findings from the BMC Clinical Data Warehouse by performing a manual chart review. We evaluated the frequency of use of opioid treatment contract and urine drug testing, in addition to number of patients receiving early refills of the opioid medication.

Methods: We conducted a retrospective review of data abstracted from electronic medical records of the patients receiving chronic opioid therapy at BMC primary care clinics. 99 Patients receiving chronic opioid therapy (defined as 3 or more opioid prescriptions written at least 21 days apart over six months) for chronic non-cancer pain during the period of 9/1/11-8/31/12 were included. We defined an early refill as an opioid prescription written 7-25 days after a previous prescription for a drug of the same name.

Results: 50 of 99 patients (50.5%) had ever had a documented opioid treatment contract. 77 patients (77.8%) had 1 or more urine drug tests and 46 patients (46.5%) had 1 or more early refills of the opioid prescription during the 1 year period of 9/1/11-8/31/12. A total of 102 early refills were documented during the same period.

Conclusions: Of the patients receiving chronic opioid therapy in a primary care setting, more patients had urine drug testing compared to an opioid treatment contract. About half of the patients had 1 or more early refills of the opioid prescriptions which may indicate potential misuse. Whether higher use of opioid treatment contracts and urine drug testing leads to a decreased number of early refills, possibly indicating decreased misuse, remains to be explored.

Sepsis: It's Going To Get You! (Diagnostically)

Aaron Kirkpatrick, MD, Allan Walkey, MD

Introduction: Outcomes of patients with severe sepsis are in part determined by timely initiation of antibiotics. Though providers cite in survey studies that difficulty with recognizing sepsis is a major factor in treatment delays, the number of patients with delays in treatment from failure to recognize severe sepsis is unclear. Early Goal Directed Therapy has improved mortality rates in severe sepsis and septic shock. In addition, time to antibiotics has also proven to be important. Many studies have focused on the treatment of sepsis/severe sepsis, however not many studies have focused on the recognition of these conditions.

Methods: We performed a retrospective, single-center, observational chart review of 110 adult medical patients admitted from 2008-2010 with a sepsis diagnosis based on *ICD-9-CM* codes 995.91, 995.92, and 785.52 who did not survive their hospitalization. We excluded patients who did not meet criteria for severe sepsis, patients that received antibiotics prior to the onset of severe sepsis, and patients who were admitted directly to the ICU from the Emergency Department for severe sepsis. Two investigators determined timing of severe sepsis onset, established when 2 SIRS criteria, suspected infection, and evidence of organ failure defined by Sequential Organ Failure Assessment (SOFA) score > 2 all occurred within a 24 hour time period. We defined a diagnostic delay *a priori* as when severe sepsis criteria were met, but physician notation of a severe sepsis diagnosis and/or antibiotic orders were not documented within 6 hours of severe sepsis onset. 35 patients met criteria.

Results: We did not identify statistically significant differences in severe sepsis diagnostic delays based on demographics. Of the patients with severe sepsis, 12 (34%) had a greater than 6 hour delay in recognition or treatment of severe sepsis; in 7 patients delays exceeded 12 hours after the onset of severe sepsis. Notably, 4 patients had antibiotics ordered greater than 1 day after criteria for severe sepsis was met.

Conclusions: In summary, significant delays in recognition of severe sepsis occurred in approximately 1/3 of patients who died during their hospitalization with severe sepsis. There was a statistically significant difference in the amount of tachycardia between the delayed recognition group and appropriate recognition group, while no significant difference was found for the other SIRS criteria. A strong trend toward nodal blocking agents and delayed recognition of severe sepsis was also noted. There was no significant difference in end organ damage between the two groups.

Discussion: This small pilot study showed that recognition of sepsis/severe sepsis needs to be improved. A Structured Observation of Clinical Skills card has been developed to help students identify sepsis. Future studies include a potential prospective cohort study to investigate barriers to recognition of sepsis/severe sepsis. Also, a retrospective study analyzing which components of SIRS criteria were present for patients with severe sepsis could help look at the incidence of tachycardia and use of nodal blocking agents. Outcomes in treatment of sepsis/severe sepsis have improved because of Early Goal Directed Therapy and Time to Antibiotics, but there still needs to be improvement in the recognition of sepsis/severe sepsis.

The cross-sectional associations of albuminuria and C-reactive protein with functional disability in older adults with diabetes mellitus

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OBJECTIVE: To examine the relationship between albuminuria, inflammation, and disability in older adults with diabetes.

RESEARCH DESIGN AND METHODS: Data were from 1729 adults (≥ 60 years) with diabetes in the National Health and Nutrition Examination Survey, 1999-2008. Disability in activities of daily living (ADL), instrumental activities of daily living (IADL), leisure and social activities (LSA), general physical activities (GPA), and lower extremity mobility (LEM) was obtained from self-report. Urinary albumin-to-creatinine ratio UACR (mg/g) was categorized into normal (UACR<30 mg/g), microalbuminuria (UACR 30-300 mg/g), and macroalbuminuria (UACR>300 mg/g). C-reactive protein (CRP) levels were quantified by latex-enhanced nephelometry.

RESULTS: In the full-adjusted model, microalbuminuria was associated with disability in ADL, LSA, and LEM with corresponding odds ratios (ORs)(95% CIs) as 1.51 (1.16-1.98), 1.62 (1.23-2.14), and 1.34 (1.03-1.74), respectively, compared with participants without albuminuria. Macroalbuminuria was associated with disability in ADL, IADL, and LEM with corresponding ORs (95%CIs) as 1.94 (1.24-3.03), 1.93 (1.23-3.02), and 2.20 (1.38-3.49), respectively, compared with participants without albuminuria. Elevated CRP (>0.3 mg/dL) was associated with increased odds of disability in ADL and LEM, with corresponding ORs (95%CIs) as 1.28 (1.00-1.62) and 1.68 (1.34-2.11), respectively. Subjects with both albuminuria and elevated CRP had higher odds of disability compared to those with no albuminuria and normal CRP.

CONCLUSIONS: Albuminuria and inflammation were independent correlates for disability among older adults with diabetes. There was an interaction of albuminuria and elevated CRP on disability, suggesting that the presence of sub-clinical inflammation may amplify the effect of albuminuria on disability in older adults living with diabetes.

Treatment of Pulmonary Hypertension associated with Diastolic Dysfunction with Iloprost: A Pilot Study

Nicole Landzberg, MD

Introduction: Nearly two thirds of individuals with elevated pulmonary arterial pressures (PAP) have pulmonary venous hypertension (PH) from left heart disease. While there are extensive data with which to develop current guidelines for treatment of pulmonary arterial hypertension (PAH; WHO Group 1), there are little data on the treatment of WHO Group 2 PH. Iloprost, an inhaled synthetic prostacyclin analogue, improves hemodynamic and clinical status with minimal systemic adversity in patients with PAH; thus in Group 2 PH patients, it might be effective with fewer adverse events. We report the results of a proof of concept study investigating the potential role of iloprost in patients with Group 2 PH associated with heart failure with preserved ejection fraction (HFpEF).

Methods: Patients referred to Boston Medical Center's Pulmonary Hypertension Center for initial evaluation of suspected pulmonary hypertension were considered for inclusion. Initial screening criteria were age 21-85, NYHA functional class III-IV, and an echocardiogram demonstrating a pulmonary artery systolic pressure (PASP) >50mmHg, left ventricular ejection fraction (LVEF) >50%, and no significant valvular disease. Subjects were invited to participate if they had a mean PAP >25mmHg, pulmonary capillary wedge pressure (PCWP) >18mmHg and <30mmHg, and pulmonary artery diastolic pressure to PCWP gradient <10. They received a test dose of 2.5mcg inhaled iloprost, followed by two subsequent doses of 5mcg. Hemodynamic measurements were recorded for each inhalation after 15, 30, 60, and 90minutes. Results were analyzed via SAS v9.3.

Results: Nine consecutive patients met demographic and clinical conditions for study inclusion. 8 subjects fulfilled the hemodynamic criteria and elected to enter the study; one patient was excluded after right heart catheterization because of a PCWP >30. While reduction of PAP (-4.71 to -7mmHg, $P<0.03$) and PVR (-95 to -163dyn·s/cm⁵, $P<0.02$) was noted with all doses of administered iloprost, the greatest effects were noted after the first inhalation of 5mcg. No significant change was noted in oxygen saturation, PCWP, CO, or SVR. All patients completed the three cycles of iloprost administration; no patient experienced pre-established criteria nor side effects sufficient to terminate the protocol with any dose of iloprost.

Conclusion: Our data demonstrate that inhaled iloprost results in acute reduction of pulmonary arterial pressure and pulmonary vascular resistance in patients with PH and HFpEF.

Correlation between tubular atrophy and interstitial fibrosis on renal biopsy and progression to ESRD

Carol Lee, Hanni Menn-Josephy, Andrea Havasi (advisor)

Intro: Although most forms of progressive, non-cystic renal disease are glomerular in etiology, previous studies have suggested that it is actually the intensity of accompanying histologic injury in the tubulointerstitium that predicts decline in renal function. For this reason, it is a well-accepted practice to examine the percentage of tubular atrophy and interstitial changes on renal biopsy to help predict the trajectory in a patient's clinical course and ascertain whether a patient would be more suited for further medical therapy versus preparation for more immediate dialysis and progression to ESRD. However, the outcomes of clinical practice suggest that interpretations of findings on renal biopsy may be more nuanced than previously thought: some patients with severe changes on renal biopsy avert the need for dialysis for many years, while others with less severe changes may become chronically dialysis dependent within months.

Methods: We carried out a retrospective analysis of 175 renal biopsies conducted on male and female adult patients at Boston Medical Center between January of 2008 through July of 2012. All biopsies were included irrespective of indication unless the biopsy occurred in a transplanted kidney or in a patient who later had a transplanted kidney during the study period. Potential covariates were obtained at the time of biopsy and included basic demographic information (gender, age, ethnicity), initial creatinine, degree of proteinuria, comorbid medical conditions (hypertension, diabetes, CAD), and final biopsy diagnosis. The primary end-point was time to initiation of chronic hemodialysis or peritoneal dialysis from the date of a patient's last renal biopsy. Based on this data, we developed dialysis predication models and assessed discrimination using AUC of the ROC curve.

Preliminary Results: Based on creation of prediction models using bivariate analyses at the 0.2 level, several baseline characteristics in conjunction were predictive of progression to dialysis: age, BMI, percentage of tubular atrophy and interstitial fibrosis, GFR at time of biopsy, degree of proteinuria at time of biopsy, and presence of hypertension - with high discriminatory ability (AUC-ROC, 0.938). The percentage of tubular atrophy and interstitial fibrosis alone was also predictive of progression to chronic dialysis (OR 1.0628, $p < 0.0001$) with moderate discriminatory ability (AUC-ROC 0.847).

Preliminary Conclusion: Based on preliminary analyses, it appears that the severity of histologic changes noted in the tubulointerstitium, may be one of several factors that have some prognostic value in determining a patient's need for chronic dialysis.

Kidney stone formation in a patient with an increased protein-rich diet.

Peter Luo

Decades of weight loss dieting trends have led to increases in dietary protein intake by individuals for weight loss management. Awareness of protein as a weight loss aid in its properties to satisfy hunger than either fats or carbohydrates, as well as ability to maintain lean muscle mass, have led to individuals habitually consuming dietary protein in excess of recommended daily intake. Excessive protein intake is certainly a health concern in individuals with pre-existing kidney disease, as there is research showing how high protein intake may initiate or promote kidney injury by chronically increasing glomerular pressure and causing hyperfiltration.

I herein report a case of a 53-year-old man who presented to our hospital with epigastric pain, and found to have radiographic studies to have right-sided hydronephrosis and an obstructing ureteral stone in the setting of an low-carbohydrate and increased protein intake diet. In this case study, I highlight the nature of this propensity of increased dietary protein for kidney stone formation and its pathogenesis, and organize available studies to clarify whether protein-induced changes in renal function are a normal adaptative mechanism within the functional limits of a health kidney, or whether there are real consequences of high protein intake on renal function.

Conflicting studies regarding the implications of high dietary protein in kidney stone formation complicate constructing universal guidelines for recommended protein intake. Some have shown that preexisting metabolic abnormality must exist before dietary protein can exert an effect on stone formation. For now, there is not sufficient evidence substantiating

A rational approach to medical marijuana

Adam Lurie, MD

The use of cannabis in the United States, whether for recreational or medical use, has been a controversial topic recently due to changes in the sociopolitical landscape. With the recent enactment of House Bill 3885 in Massachusetts by its citizens ("An Act for the Humanitarian Medical Use of Marijuana"), I have been confronted by both my patients and colleagues on the circumstances under which a physician can consider the prescription of cannabis the most appropriate therapy for a particular illness. My talk first examines the legal history of cannabis use in the United States and the motivating forces that resulted in its classification as a Schedule I substance by Congress in 1970. It then explores how the addictive nature and risk for abuse of cannabis can objectively be compared to other popular scheduled substances, and legal substances, in an effort to build a logical framework on how medical marijuana may be more appropriately rescheduled under US drug policy. I then analyze how this argument is taken beyond that of an exercise in logic, to the clinical applications of cannabis by delving into the psychopharmacology of the main components of marijuana and the (limited) data on its use in the clinical setting. Furthermore, I discuss the novel perspective of the financial benefits of legal marijuana sale, beyond that of medical usage, to justify its potential value to an idealized local community. Finally, I suggest to the audience that marijuana should be viewed through the same "riskvsbenefitlens" that we apply to any treatment we prescribe to our patient with chronic, debilitating diseases.

A novel case of Multiple Myeloma treated with Intravenous Immunoglobulin (IVIG)

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Introduction: IVIG is currently used for the prevention of recurrent life-threatening infections and has not been studied as a therapeutic agent for myeloma. We describe a case where monthly IVIG induced a sustained hematologic response in the treatment of myeloma.

Case Description: A 62 year old gentleman with asymptomatic IgG kappa smoldering myeloma diagnosed in March 2001 was being closely monitored for progression of his disease as he refused initial treatment. His baseline laboratory value were IgG 5.3 gm/dL, beta-2 microglobulin 3.49 mg/dL, mild anemia (hematocrit 37%), normal calcium, and normal kidney function. In July 2002, he was noted to have progressive disease with a rise in IgG fraction to 6.6 gm/dL with worsening anemia and agreed to treatment with pulse dexamethasone. After an initial response, the patient had a slow biochemical relapse over the next year with IgG returning to 6.1 gm/dL. Dexamethasone was then discontinued and the patient was started on thalidomide therapy. The patient had a subsequent modest response however quickly developed a life threatening pneumonia requiring intubation and prolonged hospitalization. Monthly IVIG (24 grams) infusions were started in October 2003 after gradually reinitiating thalidomide and coinciding with his return to goal dose of 200mg. IgG fraction drawn prior to IVIG administration was 7.1 gm/dL. Over the subsequent two months the patient had serious side effects of symptomatic bradycardia, volume overload, and peripheral neuropathy and discontinued thalidomide. Remarkably, the IgG fraction dropped from 7 gm/dL to 2gm/dL after two doses of IVIG and two months of goal dose thalidomide. As it was not clear if this response in IgG fraction was related to the late effects of thalidomide or to IVIG, thalidomide was cautiously restarted again but soon discontinued due to persistent severe side effects. Monotherapy with IVIG was continued from March 2004 over the next five years with a sustained biochemical response of IgG fraction (ranged from 2 gm/dL to 4 gm/dL) until subsequent progression in August 2009.

Discussion: Accumulating evidence has demonstrated the bone marrow microenvironment, immune dysfunction, and immune evasion are critical components in the pathobiology of myeloma. These include abnormalities of dendritic cells (DC) and T regulatory cells (Treg), and of increased secretion of proangiogenic cytokines such as interleukin (IL)-6, transforming growth factor (TGF)- β , vascular endothelial growth factor (VEGF), and hepatocyte growth factor (HGF) by the bone marrow stromal cells. The response rates to immunomodulators such as thalidomide and lenalidomide further highlight myeloma mediated immune dysfunction as a therapeutic target for research. We suspect the response to IVIG in this case is due to beneficial immune regulatory effects that have been shown in other experimental and clinical settings with T regulatory cells likely playing a central yet undefined role. Further research is needed to elucidate this effect.

Mechanisms of Blimp-1 Mediated Repression of HIV Provirus

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Objective: Understanding the establishment of HIV-1 latency by recruitment of histone deacetylases (HDACs) and methyltransferases (HMTs) is imperative to developing therapies that will fully eradicate HIV infection. Blimp-1, a key transcriptional regulator of effector and memory differentiation represses T-cell specific genes by recruiting HMTs, such as G9a. We propose that Blimp-1 represses HIV transcription by recruiting chromatin modifying complexes. **Methods:** T cell lines stably expressing Blimp-1 or shRNA that knockdown Blimp-1 were infected with HIV and treated with either BIX01294, a specific inhibitor of G9a, or TSA an HDAC1 and 2 inhibitor, followed by activation by CD3+28. HIV transcription and replication were monitored. **Results:** We demonstrated that Blimp-1 overexpression repressed HIV-1 proviral transcription, while inhibition of Blimp-1 mediated increased HIV-1 transcription. BIX01294 nor TSA were not able to overcome BLIMP-1 mediated repression of HIV transcription.

Conclusion: These results confirm that Blimp-1 represses HIV-1 transcription. In addition, Blimp-1 repression of HIV-1 does not appear to require the recruitment of G9a or HDAC1,2, but rather may recruit other unknown chromatin modifiers not yet explored. We propose a model for a role in which Blimp-1 limits HIV in different T cell subsets.

Healthcare Payment Models and Accountable Care Organizations

Chris Morrison, MD

The United States spends more money per capita on healthcare than any other nation in the world. Despite this, life expectancy is ranked 42nd in the world and child mortality is higher than many other developed nations. The current reimbursement model of fee-for-service incentivizes a high volume of services without regard to the quality of care provided. Additional models of healthcare payment may be able to encourage more efficient use of healthcare resources.

Accountable care organizations (ACOs) are healthcare delivery models that integrate numerous providers and services. ACOs are tasked with reducing expenditures and meeting certain clinical quality measures. Medicare provides monetary bonuses or penalties based on whether or not the ACO meets these tasks. ACOs may not, however, be a panacea. For instance, they are costly to implement for most non-integrated practices, may not result in significant savings, and may select for certain patient populations.

Single Center Simulation-Based Training of Cardiopulmonary Resuscitation for Internal Medicine Residents

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BACKGROUND: Internal Medicine (IM) residents lead “code blue” or cardiopulmonary resuscitation events at most academic centers. Literature demonstrates increased confidence of code leaders leads to better clinical outcome. However, current training and experience in managing code blue events is insufficient. Our study investigated changes in confidence, competence and knowledge of IM residents after implementation of a multidisciplinary simulation-based cardiopulmonary resuscitation code leadership training at Boston Medical Center (BMC).

METHODS: The training occurred in BMC’s Solomont Center for Clinical Simulation and Nursing Education. It involved a didactic session on code blue management with focus on communication and leadership skills followed by simulated code blue scenarios and debriefing with facilitators. The curriculum was collaboratively designed with simulation center staff and senior faculty members of the Divisions of Cardiology and Critical Care. Residents were administered pre- and post-training surveys on self-assessment of confidence, competence and knowledge of code blue leadership. All survey results were double-entered using REDCap to eliminate any data-entry errors prior to analysis. Matched data was generated and McNemar’s exact test was used for analyses.

RESULTS: A total of 49 residents completed both surveys, of which 15 residents had a chance to lead actual codes between the 2 surveys. There was a statistically significant increase in the reported level of knowledge regarding code leadership (n=31, pre=51.6%, post=77.4%, p=0.02). Additionally, there was a positive trend, without reaching statistical significance, in confidence (n=15, pre=40%, post=67%, p=0.125), comfort (n=32, pre=40.6%, post=56.3%, p=0.18), and competence (n=32, pre=53.1%, post=62.5%, p=0.51) to lead a code. In both pre- and post-test surveys, residents reported identifying themselves as a code leader at a high rate (n=15, pre=87%, post=93%, p=1.00). Feedback from residents was notable for requests for more frequent simulations.

CONCLUSIONS: Simulation-based training increases residents’ perceived level of knowledge required to successfully lead codes. Other variables evaluated including comfort, competence and confidence trended positive as well.

Targeted therapy in oncology

Prabhjot S. Mundi

Conventional chemotherapy often provides limited and short lived response rates in many advanced solid (and some liquid) malignant neoplasms that are beyond the stage of surgical cure. Conventional chemotherapeutic agents in general effect individual phases of the cell cycle, and result in significant toxicity to organ systems that rely upon continuous cell division to maintain homeostasis. Conventional chemotherapy is also unable to effectively target quiescent tumor stem cells, which are thought to be a source of tumor recurrence even when radiographic complete response is achieved. Targeted therapy in oncology refers to agents, often synthetically derived, that target specific molecular pathways involved in tumor progression. The four cardinal properties of malignant tumors are uncontrolled cellular proliferation, invasiveness, angiogenic switch, and metastasis. These four processes progress and adapt in a non-linear, parallel fashion, and represent important targets in the development of novel anti-neoplastic agents. In spite of the seemingly exponential increase in the number of available targeted therapies at the clinical level in recent years, there have been a disappointing lack of meaningful advances. As our knowledge of tumor genetics, epigenetics, proteomic signatures, and the ability of malignant cells to recruit and transform non-malignant cells into essential components of the tumor milieu continues to expand, a commitment to rigorous scientific principles at the pre-clinical level will allow for more rapid breakthroughs. Future directions in targeted therapy will include early molecular characterization of individual tumors, allowing for the appropriate selection of multiple targeted agents that will maximize tumor effect and minimize adverse effects to healthy tissues. Conventional measures of tumor response rate, such as decrease in tumor diameter on radiographic studies or reduction in tumor burden on bone marrow biopsies, may not be appropriate measures of response rate for targeted agents. Likewise, conventional measures of acute therapeutic toxicity such as neutropenia and gastrointestinal effects may be replaced by more subtle but permanent adverse effects of targeted therapies that patients may be using for the remainder of their lives.

Pneumocystis jiroveci pneumonia in patients with inflammatory bowel disease: a survey of prophylaxis patterns among gastroenterology providers

Philip N. Okafor MD MPH, Sharmeel K. Wasan MD, Francis A. Farraye MD MSc

Background: The use of combination immunosuppressive agents is associated with reports of pneumocystis jiroveci pneumonia (PJP). The aim of this study was to determine practice patterns among gastroenterology providers for PJP prophylaxis in patients with inflammatory bowel disease (IBD) on immunosuppressive therapy.

Methods: An internet-based survey of 14 questions was sent through e-mail to a random sampling of 4000 gastroenterologists, nurse practitioners, and physician assistants between November 2011 and February 2012. Three reminder e-mails were sent to providers who had not completed the survey.

Results: The invitation e-mail that contained the link to the survey was clicked by 504 providers and the completed surveys were returned by 123 of them (78% physicians, 11% nurse practitioners, 11% physician assistants). The response rate was 24.4%. Seventy-nine percent of the respondents had managed >25 patients with IBD in the past year, with as much as one-third of all respondents managing >100 patients. Eight percent of the respondents reported patients who had developed PJP on immunosuppressive therapy, 11% reported initiating PJP prophylaxis, mostly for patients on triple immunosuppressive therapy. Prescription of PJP prophylaxis was not significantly associated with the number of years in practice or the number of IBD patients treated. However, providers with patients that had developed PJP were 7.4 times more likely to prescribe prophylaxis ($P = 0.01$). In addition, providers in academic centers were 4 times more likely to initiate PJP prophylaxis than those in nonacademic centers ($P = 0.03$). The most common reasons for not prescribing PJP prophylaxis included the absence of guidelines on the benefits of prophylaxis, lack of personal experience with PJP, and the lack of knowledge on the need for prophylaxis in patients with IBD on combination immunosuppressive therapy.

Conclusion: The lack of guidelines seems to influence the decision on not to prescribe PJP prophylaxis in patients with IBD. Additional studies are needed to determine PJP risk factors and risks and benefits of prophylaxis.

Cost-Effectiveness of Nonmelanoma Skin Cancer Screening in Patients with Crohn's Disease

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Background: Several studies have demonstrated an increased risk of nonmelanoma skin cancer (NMSC) in inflammatory bowel disease patients, with the greatest risk in Crohn's disease (CD) patients. We investigated the cost-effectiveness of NMSC screening in CD patients.

Methods: A mathematical model was used to compare lifetime costs, life expectancies and benefits of NMSC screening in a hypothetical cohort of 100,000 CD patients. Strategies studied include: i) Treat NMSC cases as they present and follow affected patients annually ii) Screen CD patients annually once they turn 50, treat NMSC cases as they present and follow affected patients annually iii) Screen CD patients annually once they start receiving thiopurines, treat NMSC cases as they present and follow affected patients annually iv) Screen CD patients annually when they turn 50 or start receiving thiopurines, treat NMSC cases as they present, and follow affected patients annually v) Screen all CD patients annually. These strategies were then studied on a biennial basis, accounting for 10 competing strategies.

Results: The total lifetime cost of caring for patients with CD ranged from \$22,647 to \$597,838, with a mean cost of \$328,247. Screening all CD patients annually proved the most cost-effective strategy with an average lifetime cost of \$333,193, a quality adjusted life expectancy of about 26 QALYs (95% CI: 22–29), and an incremental cost-effectiveness ratio of \$3,263/QALY. This strategy led to early detection of about 94% of incident NMSC cases. The next best strategy involved screening all CD patients biennially and was associated with an average lifetime cost of \$328,312 with 24.5 QALYs (95% CI: 21–25). However, only 47% of new NMSC cases were detected early with this strategy.

Conclusion: At a willingness-to-pay threshold of \$50,000, screening all CD patients annually for NMSC proved the most cost-effective strategy.

Increased risk of pneumocystis jiroveci pneumonia among patients with inflammatory bowel disease

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Background: Patients with inflammatory bowel disease (IBD) may be at increased risk for pneumocystis jiroveci pneumonia (PCP). Our aims were (1) to determine the incidence and relative risk of PCP in IBD and (2) to describe medication exposures in patients with IBD with PCP.

Methods: We performed a retrospective cohort study and a case series using administrative data from IMS Health Inc, LifeLink Health Plan Claims Database. In the cohort, patients with IBD were matched to 4 individuals with no IBD claims. PCP risk was evaluated by incidence rate ratio and adjusted Cox proportional hazards modeling. The demographics and medication histories of the 38 cases of PCP in patients with IBD were extracted.

Results: The cohort included 50,932 patients with Crohn's disease, 56,403 patients with ulcerative colitis, and 1269 patients with unspecified IBD; matched to 434,416 individuals without IBD. The crude incidence of PCP was higher in the IBD cohort (10.6/100,000) than in the non-IBD cohort (3.0/100,000). In the adjusted analyses, PCP risk was higher in the IBD versus non-IBD cohort (hazard ratio, 2.96; 95% confidence interval, 1.75-4.29), with the greatest risk in Crohn's disease compared with non-IBD (hazard ratio, 4.01; 95% confidence interval, 1.88-8.56). In the IBD case series of PCP cases (n = 38), the median age was 49 (interquartile range, 43-57). A total of 20 individuals (53%) were on corticosteroids alone or in combination with other immunosuppression.

Conclusion: Although the overall incidence of PCP is low, patients with IBD are at increased risk. Patients with IBD with PCP are predominantly on corticosteroids alone or in combination before PCP diagnosis.

A CURIOUS CASE OF LACTOBACILLUS CASEI IN A PROSTHETIC JOINT: WAS IT THE YOGURT?

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Intro: Infection with *Lactobacillus* is uncommon.

Case description: 95-year-old woman with hypertension, diabetes mellitus, coronary artery disease, chronic systolic heart failure, and dementia who underwent a left total hip replacement after a fall resulting in a displaced intertrochanteric fracture of the left proximal femur 1.5 years before admission. She was admitted to the hospital with a stage III ulcer along the lateral aspect of her left thigh, erythema, and a moderate amount of serosanguinous drainage. Vitals were stable, and labs were remarkable for an elevated CRP. Despite antibiotic therapy, her WBC rose to 15,000/L, and she developed a low-grade fever with increasing somnolence. She was taken to the operating room where she underwent extensive debridement of the left hip, excision of a sinus tract, and modular exchange of the hemiarthroplasty components. Superficial wound cultures grew methicillin-sensitive *Staphylococcus aureus* (MSSA). Deep cultures from the initial ultrasound-guided aspiration fluid and the intracapsular synovium grew *Lactobacillus* species, identified as *Lactobacillus casei* and *L. paracasei*. She completed 4 weeks of intravenous penicillin G followed by a prolonged course of suppressive therapy with oral dicloxacillin because her femoral hardware remained in place and could not safely be exchanged. She improved on this regimen and at her last visit was ambulating with a walker, which was her pre-morbid functional baseline.

Discussion: *Lactobacilli* are gram-positive, nonmotile, nonsporeforming anaerobes or facultative anaerobes, generally found as commensals in the gastrointestinal tract and vagina. The medical literature cites case reports of *L. casei* and *L. paracasei* causing septic arthritis of a native shoulder and a prosthetic knee, splenic abscess, liver abscess, pancreatic necrosis, endocarditis, and peritoneal dialysis-related peritonitis. Although these cases have generally occurred in relatively immunocompetent individuals, the majority had diabetes mellitus, as did our patient. We believe that this is the first reported case of a prosthetic hip infection with *L. casei* and *L. paracasei*.

On review of our patient's supplements and yogurts, the yogurt she ate at the rehabilitation facility and at home contained *L. casei*. Whether her wound was inoculated with *L. casei* and *L. paracasei* from her food or from local spread from gut or vaginal flora is unknown, although it is a curious finding.

Clinical Documentation - Lost Art or New Science?

Thomas Ostrander

Abstract: The technique, scope, and purpose of clinical documentation has evolved significantly over time. Efforts to mandate and standardize physician documentation of clinical encounters originated in the early 20th century, first with the Flexner Report and later through the efforts of the American College of Surgeons. For most of the last century, physician documentation consisted of random, haphazard summaries of the thoughts and activities of physicians regarding their patients. This was revolutionized in the latter 20th century by two factors – Weed's Problem-Oriented Medical Record (POMR) and the emergence of Electronic Health Records (EHR). Weed introduced the POMR as a vehicle for broad change in everything from the quality of care delivered to the ability to use patient data for research. While the POMR concept and format has been widely adopted, the rise of EHR has had even greater impact on modern clinical documentation. EHR has led to great improvements in the accessibility and quality of available information, but it has also created significant new challenges. This has implications for everything from performance measures to reimbursement to how medicine itself is practiced. As EHR proliferates at the direction of public policy and through market forces, modern physicians continue to be carried by the currents of change, rather than having an organized impact on its direction.

Vitamin Deficiency: A Sticky Situation

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A 59 year old male with a history of Type II diabetes and hypertension presented with dizziness and a fall. The patient was unable to give much of his own history as he was initially slow to answer and often did not give answers to questions asked. From his family, he was noted in the past couple of months to be more withdrawn. Physical exam noted a cachectic Haitian male with a flat affect. He was alert and oriented to person, place, and time but re-call was very prolonged. His cranial nerves were intact. His muscle strength was 4/5 in both his upper and lower extremities. He had diminished sensation to light touch, + Romberg, ataxia and wide based gait. Reflexes were 1+ in lower extremities. Laboratory studies revealed pancytopenia with a hematocrit 23.4%, MCV 86, reticulocyte 0.8%. A peripheral smear, unfortunately after blood transfusions, revealed hypersegmented neutrophils and ovalocytes. Further studies yielded normal iron levels, normal folate level, low B12 <146 pg/ml (normal 213-816 pg/ml). elevated methylmalonic acid 39680 nmol/L (normal 87-318 nmol/L) and homocysteine 198.1 umol/L (normal 6-16 umol/L). Intrinsic factor and gastric parietal cell antibodies were positive. Endoscopy showed chronic atrophic gastritis. Pan CT scan noted a thyroid nodule and also incidental subsegmental pulmonary embolus.

The patient was initiated on low molecular weight heparin and warfarin and plan was to anticoagulate him for 6 months. As the patient was not noted to have any prior history of venous thromboembolism (VTE) nor any family history of VTE and felt to have a reversible risk factor identified, full hypercoagulable workup was deferred. He was also started on daily B12 injections for 1 week with instructions to transition to weekly injections for 1 month and then monthly injections. He was discharged to a nursing facility and subsequently returned in 2 days after noticing a hematocrit drop with INR 1.92. He was found to have a retroperitoneal and right iliopsoas bleed as well as deep vein thromboses in his left lower extremity. His warfarin was reversed with FFP and vitamin K. He was given PRBC and an IVC filter was placed with plan to resume anticoagulation pending a discussion of its risks and benefits.

This case illustrates hyperhomocysteinemia from pernicious anemia as a possible cause of VTE. Prior studies have shown an association between homocysteine and both arterial and venous thrombosis, however no official guidelines exist as to who should be tested for hyperhomocysteinemia. There are also a few case studies noted of VTE associated with pernicious anemia in the setting of elevated homocysteine levels. Although the treatment for hyperhomocysteinemia is relatively easy, the VITRO study has shown no evidence that decreasing homocysteine levels with folic acid, vitamin B6, and vitamin B12 supplements lowers the incidence of recurrent thrombosis. It is notable that our patient had much higher homocysteine levels (198.1 umol/L) than the level needed to be classified as having hyperhomocysteinemia in the VITRO study (mean 15.1 umol/L, range 6.3-84.8 umol/L), and further studies would need to be performed to determine if patients with severely elevated homocysteine levels benefit from homocysteine reduction through vitamins to decrease risk of VTE formation.

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A Survey of Residents on Discharge Medication Reconciliation Practices

Helen Tang Paradise, MD MPH

Background: Medication reconciliation is a complex process, and various factors can lead to errors and result in increased patient morbidity and decreased patient satisfaction.

Purpose: To determine current practice patterns with regard to discharge medication reconciliation among residents and to uncover some of the problems encountered in the process.

Methods: During March-April 2013, a survey was distributed among 145 internal medicine residents at Boston Medical Center. The survey included seven multiple choice questions and one open-ended question regarding problems and assumptions encountered during the discharge medication reconciliation process. The answer options were “never,” “rarely (1-2 times per year),” “infrequently (1-2 times per month),” “sometimes (1-2 times per week while on service),” “frequently (almost daily),” and “always.”

Results: Of 145 residents, 32 (22.1%) responded to the survey including 11 interns, 9 juniors and 12 seniors. Fifteen (46.9%) residents reported “frequently” or “always” assuming medication reconciliation was properly done during admission. Eight (25.0%) residents reported “frequently” or “always” discharging a patient they did not admit without reconfirming medication names and doses, but 53.1% of residents reported “never,” “rarely,” or “infrequently” doing so. The majority of residents (78.1%) reported that a challenge was that patients “frequently” or “always” did not know what medication they were taking. When external sources needed to be contacted for medication verification, 32.3% residents reported “sometimes,” “frequently,” or “always” failing to contact family for information, and similar percentage (34.4%) of residents failed to contact the pharmacy. No resident reported “frequently” or “always” failing to update Logician (outpatient medical record system) medication list when discrepancies occurred, but only 21.9% of residents “never” failed to update Logician.

Residents cited many challenges during the medication reconciliation process including mistakes in patients' recall of medication names or doses, patients' low health literacy, the lack of access to certain records at night, provider mistakes, assumptions made by providers regarding the completeness of admission medication reconciliation and regarding the role of nurses in the discharge process, and the difficulty of ensuring that the correct medication was obtainable and obtained by patient after discharge.

Conclusions: Residents face many challenges during the discharge medication reconciliation process. Residents frequently updated the medication list when they were aware of discrepancies, but many assumed that medication reconciliation was done properly on admission, and few frequently contacted family or pharmacy when the need existed. Residents should be taught the standard process for medication reconciliation during Intern orientation, the types of medications considered “high risk,” and practical methods for resolving problems encountered during the process. Gaps and discrepancies during admission medication reconciliation should be communicated during hand offs, and the role of nurses and pharmacists in the process should be better defined.

*Special thanks to Jane Demata, Ann Hill and Allison Marshall at BMC Patient Safety Department for supporting this project.

The need to implement a process of performing effective medication reconciliations both on admission and discharge in order to avoid adverse events during hospitalizations and transitions of care.

Payal Parikh, MD; David Thornton, MD; Jeromy Lian, MD, Jai Singh, MD

Case: Mr. WH, an 83 year old male with CAD s/p CABG, PCIs, HTN, presented with one day of altered mental status and was diagnosed with hypertensive emergency with a BP 198/90. Throughout his 4 day hospital course, multiple medication changes were made including halving of his home atenolol dose to 12.5mg qd, starting a clonidine taper to 0.1mg qd, halving Imdur to 60mg qd, adding lisinopril 10mg qd, and continuing home Norvasc 10mg qd. Additionally, his home HCTZ 25mg and Nifedipine 60mg qd were held. Four days after discharge, Mr. WH's wife called to inform the nurses that he was persistently dizzy. A detailed review of the discharge medication reconciliation revealed that HCTZ was continued on the discharge med list, he had been prescribed 0.3mg clonidine tablets instead of 0.1mg tablets, and atenolol could not be effectively cut into half. Two months later, Mr. WH was readmitted with hypertensive emergency because his wife was not comfortable implementing the medication changes given all the errors on discharge.

Problems Identified: The main problem identified in this case is that the discharge medication reconciliation was erroneous due to a lack of a proper admission medication reconciliation and discharge communication. Currently, at WXVA, one does not need to formally perform admission medication reconciliations, nor is there a set system in place to perform them. Furthermore, the current view of medication reconciliations is that they are not an important aspect of a hospital admission.

Underlying Literature: *To Err is Human* (1999) cites 45,000-98,000 patients die yearly from iatrogenic errors, and of those 7,000 are from medication errors. Furthermore, in a 2011 study performed at an urban academic VAMC, medication reconciliations were associated with fewer adverse events (odds ratio, 0.57). Finally, a 2012 study analyzing various clinician's (physicians, nurses, pharmacists) perceptions of which group is responsible for performing an effective medication reconciliation outlined that each group of clinicians named another group for this responsibility.

My proposal for improvement: I propose that effective discharge medication reconciliations rely on performing effective admission medication reconciliations and the responsibility falls on all clinicians taking care of the patient. I propose starting a new document entitled "medication reconciliation" on admission and implementing a visual key which will allow all clinicians to understand which medications are either continued (→), changed (#), added (+), or held (X) on admission, denoted by the symbols. This will create a formalized process, which will then allow for better communication both during the admission and also during transitions of care.

Title: Analysis of miR-30b (miRNA) expression data and correlation of COPD associated airway mRNA/microRNA gene expression.

Authors: Ami K. Patel, Rebecca Kusko, John F. Brothers II, Teresa Wei Wang, Joshua David Campbell, John Tedrow, Daniel Kass, Kusum V. Pandit, Luai Hukeihel, Naftali Kaminski, Stephen Lam, Mark Lenburg, Avrum Spira, and Katrina Steiling

Mentor: Katrina Steiling, MD

Field: Bioinformatics/Computational Medicine

Background: Computational medicine encompasses the application of genomics and bioinformatics tools to the translational study of diseases with the goal of developing new diagnostic methods and therapeutics that can be applied directly to clinical care. The objectives for this research project were two-fold, and focused on the regulatory role of microRNA expression on gene expression in the context of COPD. The first objective was to analyze in vitro expression data of miR-30b, a microRNA hypothesized to be important in the alternative splicing of genes in COPD. The second was to learn statistical and computational techniques to analyze mRNA and microRNA expression data and then link the two in vivo datasets with the goal of identifying regulatory relationships between COPD-associated microRNA and mRNA expression profiles. The ultimate goal was to be able to describe the relationship between COPD associated airway microRNA expression versus mRNA expression and examine the biological pathways behind both in an effort to better understand the molecular changes that lead to the development of COPD.

Methods: To determine the affect of miR-30b expression on gene expression, microarray data obtained from cell lines in which miR-30b was up-regulated or knocked-down were analyzed. Data quality was assessed using Principle Component Analysis (PCA). T-tests were then performed to find significantly expressed genes in each of the cell lines versus the negative control. Differentially expressed genes meeting a false discovery rate (FDR) < 0.01 were visualized using a heat map. To determine the biologic effect of miR-30b, gene expression changes induced by miR-30b over- and under-expression were analyzed via Database for Annotation, Visualization and Integrated Discovery (DAVID) and Gene Set Enrichment Analysis (GSEA). The relationship of miR-30b-induced gene expression changes with other gene expression datasets was determined using GSEA.

For the second part of this project, I explored the relationship between COPD-associated mRNA and microRNA expression datasets generated from bronchial airway epithelial cells obtained from 60 individuals with and without COPD. The expression levels of 19793 mRNA and 475 microRNA were compared using Context Likelihood Relatedness (CLR), with a false discovery rate (FDR) < 0.05 indicating statistical significance.

Results: The expression levels of 105 genes were altered with miR-30b over-expression, and 2700 genes with miR-30b knock-down (FDR < 0.01). Using DAVID, the downstream gene expression changes associated with alterations in miR-30b expression were significantly enriched in alternative splicing, suggesting that miR-30b may play a role in regulating this function (p < 0.01). Using GSEA, we further identified that the expression of genes decreased by miR-30b overexpression were enriched in the ECM pathway and the integrin pathway (GSEA FDR < 0.05).

For the second part of this project, the CLR network was filtered by selecting miR-mRNA pairs connected at CLR-FDR < 0.05, and miR that were differentially expressed in COPD. The

resulting network was visualized using Cytoscape. Using this approach, we identified microRNA differentially expressed in COPD that were negatively correlated with predicted mRNA targets. .

Conclusions: These findings suggest that, using an in vitro cell line system, miR-30b may negatively regulate mRNA that play a role in alternative splicing. These results also suggest that, in vivo, alterations in COPD-associated microRNA expression may regulate a subset of the gene expression changes associated with COPD.

“Rounding with the Sandal Doctors: Lessons learned in Hyderabad, India”

Eva Petschnigg

Abstract for Senior Talk

Introduction: We traveled to Hyderabad (India) for a three week elective in December 2011 and visited four hospitals, both public and private. During the rotation, we rounded with multiple physicians, met with the Chief Financial Officer of a private hospital as well as the main administrator of the Aarogyasri Health Care Trust and learned important lessons about the Indian health care system.

Lesson #1: Failure of public sector leads to high private spending

Overall health care expenditure in India is only 3.9% of GDP, of which 20% are financed via the public sector. Not only is government spending very low for health care, patients only use public facilities 20-40% of the time. Some of the reasons why the public sector is failing is the high rate of absenteeism and low motivation of providers. Because of the high use of private sector, patients have very high out of pocket expenses, spending up to 10 times their monthly budget on health care, allowing catastrophic health events to happen.

Lesson #2: Limited regulation of private sector leads to variability of cost and quality of care

The failure of the public system allowed private health care providers to grow rapidly and up to 70% of providers charge on a fee-for-service basis. Government unable to provide proper regulation to enforce professional conduct, control health care costs or quality of care. This leads to a large variability of prices and unqualified private doctors delivering the lowest standard of care. Furthermore, undesirable practices have developed such as over-prescription of drugs, diagnostics and surgeries.

Lesson #3: Public-private partnerships allow for health care reform and new innovations

In recent years, local governments have developed health insurance schemes that use public funding to cover below poverty level families for catastrophic health events such as surgery or hospitalizations. Under the scheme, premium is paid by the government, but patient may choose to use public and private sector. Scheme has been expanded to national level with great success as it is portable, paperless and cashless. It has improved coverage, access and infrastructure and decreased out of pocket costs. Challenges include fraudulent claims, absence of primary care coverage and low utilization.

Finding Conn's, and Life After

Irene Rahman, Mentors Craig Gordon, Teresa Cheng

Learning Objectives

1. Understand the initial workup for Conn's syndrome
2. Understand the confirmatory workup for Conn's syndrome when the initial workup is ambiguous.
3. Recognize that despite treatment for secondary hypertension, patients may still have underlying essential hypertension.

Case Presentation: The patient is a 62 year old man with a history of long-standing hypertension and diabetes who was noted to have persistent hypokalemia despite being on potassium supplementation. His anti-hypertensive regimen at presentation included lisinopril 40mg daily, labetalol 300mg daily and amlodipine 10mg daily, with ambulatory systolic blood pressure readings in 140-160 mmHg range. The patient reported getting leg cramps often, but otherwise review of systems was negative. Physical exam did not reveal any stigmata of the secondary causes of hypertension. Metabolic panel showed potassium of 3.4 mmol/L while on 40mEq of supplement daily. Plasma aldosterone concentration (PAC) and plasma renin activity (PRA) were 19 and 0.17 respectively, with a ratio of 112. Saline suppression test was performed, in which the patient's aldosterone level suppressed to 6ng/dL after 4 hours of saline infusion. CT imaging revealed two 8-9mm nodules in the left adrenal gland. Adrenal vein sampling showed aldosterone to cortisol ratio 4.66 times higher on left side compared to right side. Patient was referred to surgery, and underwent a left adrenalectomy. Post-operatively, patient had systolic blood pressure in 140 mmHg range, for which amlodipine was continued.

Discussion: In this patient with persistent hypokalemia and hypertension, a work up for primary hyperaldosteronism was indicated. The initial approach was to determine the plasma aldosterone concentration (PAC) and plasma renin activity (PRA). In a population with a prevalence of the disease of 20%, the combination of PAC > 20 ng/dL and PAC/PRA > 30 has sensitivity and specificity of 90% for detecting aldosterone producing adenoma. Our patient was only noted to have a borderline PAC but high PAC/PRA necessitating further workup. When the results of the initial hormone levels are ambiguous, inappropriate aldosterone secretion should be confirmed by a saline suppression test, with aldosterone level suppressed to <5 for normal patients and >10 for patients with primary hyperaldosteronism, which put our patient in the gray zone again. CT imaging was performed to visually detect and distinguish between bilateral hyperplasia (~60% of cases) and unilateral adenomas (~35% of cases), the most common causes of primary hyperaldosteronism. We finally pursued adrenal vein sampling for two reasons: (1) to prove biochemically that the unilateral nodules on imaging represent functional adenomas causing primary hyperaldosteronism, also known as Conn's syndrome; (2) to justify pursuing unilateral adrenalectomy of the culprit gland.

Despite confirming that the patient's left adrenal was the culprit gland, he continued to have elevated blood pressures post-adrenalectomy, although requiring less anti-hypertensive treatment. It has been shown that hypokalemia is curable but residual hypertension persists in 43.8% of patients, which likely indicates underlying essential hypertension in addition to primary hyperaldosteronism. The pathogenesis of essential hypertension is poorly understood, but many risk factors have been identified. Those present in this patient include older age, family history, and increased sodium intake. Thus, patients with an identified cause of secondary hypertension should be followed post-treatment to monitor for essential hypertension, and treated accordingly per guidelines.

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Current Screening Practices for Incident HCV Infection among HIV Infected Patients

J. Morgan Richards, Wei Huang, Laura F. White, and Benjamin P. Linas

Introduction: The incidence of HCV infection among HIV-infected (HIV+) men who have sex with men (MSM) is rising. Little is known about current HCV screening practices for HIV-infected individuals, and data are needed to develop guidelines to inform best practice. We evaluated current HCV screening practices among US HIV-providers and identified factors associated with frequent screening.

Methods: This is a prospective cohort study that used data from the CFAR Network of Integrated Clinical Systems (CNICS). Subjects included HIV+ individuals over 18 years who enrolled in CNICS between 2000-2011 with negative HCV antibody (Ab) at baseline. We used descriptive measures and Poisson regression to identify factors associated with frequent surveillance screening for incident HCV. To test for a trend toward more frequent screening over time, we divided follow-up into 3 periods (2000-2003, 2004-2007, 2008-2011) and calculated the incidence of screening/person-year in each, allowing subjects to contribute follow-up time to one or several periods as appropriate.

Results: Among 17,090 patients who enrolled at a CNICS site during the study period, 14,534 (90.8) were screened within three months of their initial HIV visit date, 1,468 (9.2%) were screened after three months, and 1088 (6.3%) were never screened for HCV. The prevalence of chronic HCV infection at study baseline was 15.6%. Among the 12,259 patients who were HCV un-infected at baseline, 5,509 (44.9%) had HCV surveillance screening previously, and incident infection was identified in 298 (5%). In univariable analysis, factors associated with ever receiving a surveillance HCV screening test included longer follow-up time, older age, white or Asian race, self-reported history of injection drug use (IDU), and clinical site. In multivariable analysis, factors associated with a higher incidence of screening included older age, reporting a history of IDU, combination of MSM and IDU, time period, and clinic site. There was a statistically significant trend toward more frequent surveillance screening for incident HCV infection over time, though the trend was not equal at all sites.

Conclusion: Screening for prevalent HCV infection at enrollment in HIV care is quite high (>90%). There is an observable trend over time toward more frequent screening for incident HCV; however, surveillance screening is less frequent among MSM who do not report IDU, potentially missing a high-risk group. Further, surveillance screening and the rate of improvement in surveillance screening are variable between sites, suggesting a lack of routine practice. Guidelines for best surveillance screening practice are needed.

A biomimetic device for vascular permeability control in vitro

May Tun Saung, Yong-Tae Kim, Robert Langer

The endothelium has a unique role in nano-medicine in that its physiologic properties play an integral role in a wide variety of pathologic processes (e.g. increases vascular permeability in inflammation, secretes factors to cause vasodilation, serves as the site of atherosclerotic plaque formation, etc.), and it serves as the conduit that delivers the nano-therapies to target tissues. While the development of nano-particles have been expanding, there has been limited investigation into screening nanoparticles for their ability to translocate across the endothelium in order to enter the appropriate tissues. The aim of this project was to create an in-vitro microfluidic system comprised of an endothelium whose permeability could be modulated through the introduction of various endogenous factors known to increase vascular permeability, or by alteration of shear stress to imitate effects of blood flow. Our study showed that shear stress caused the endothelium in the microfluidic system to orient along the direction of flow, and that endogenous factors such as IL-1beta and thrombin increased permeability as observed on cellular imaging. More investigation is needed to better characterize nanoparticle behavior in this microfluidic system. This micro-vascular “lab-on-a-chip” can have many practical applications, including being used to determine the appropriate nano-particles for a particular clinical application prior to in-vivo use.

Patient Navigation for Screening Mammography: A Resident Clinic Quality Improvement Initiative

Swati Shroff, MD, Tracy Battaglia, MD

BACKGROUND: In an era of accountable care, health system innovations are necessary to achieve equity in quality healthcare delivery. Patient navigation (PN) has been used to address breast cancer disparities; however, its use has not been evaluated in resident training practices. This study aims to evaluate the use of PN in resident primary care clinics to improve mammography screening rates.

METHODS: We conducted a pre-post evaluation of a breast cancer quality improvement (QI) initiative from September 2011 – July 2012 at the largest ambulatory resident clinic at Boston Medical Center (BMC). The initiative began with a didactic session introducing residents to the concept of PN, including existing telephone, written, and electronic protocols navigators use for scheduling and tracking mammograms. Eligible patients for the QI initiative included: women aged 51 – 70 years of age, assigned to a resident provider, and seen by a BMC internal medicine provider within the past 2 years. The outcome of interest was mammography adherence, defined by the Healthcare Effectiveness Data and Information Set (HEDIS) measure as completion of a screening mammogram within the past 24 months. The QI initiative was designed so that all women whose last documented screening mammogram was ≥ 18 months ago received one-on-one navigator outreach and tracking over time to ensure 24 month adherence to screening mammography. Those whose last documented mammogram was < 18 months ago received usual care. Clinical and demographic data were extracted from the electronic medical record. McNemar's test was used to compare pre and post-adherence rates. An electronic self-administered post-intervention survey was administered to the residents to assess their experiences with PN.

RESULTS: 66 residents had 552 patients eligible for the QI initiative. The majority of the women were Non-White (Black 64%, Hispanic 13%), publicly insured (60%), and non-US born (62%). Pre-intervention, only 293 women (53%) were adherent to screening mammography according to the HEDIS measure. Adherent women were more likely to be Black (70% v. 58%, $p=0.002$), insured (74% v. 65%, $p=0.05$), and have a mammogram report on record (96% v. 28%, $p<0.0001$). Post-intervention adherence rates significantly improved after 9 months of implementation of PN (66% v. 53%, $p<0.0001$). Improvements were observed across all sociodemographic groups. Among the navigated group ($n=196$), 48% were unable to be contacted by phone, while only 15% declined mammography services. Of the 27 (41%) residents who completed the survey, 75% reported at least one communication with the navigator, yet only 14% knew the navigator's name. 35% felt PN decreased their workload, and 100% would like to see PN's role expanded within their ambulatory practices.

CONCLUSIONS: PN has potential to improve the equitable delivery of quality care, in this case, mammography adherence rates, among resident practices serving vulnerable populations, despite challenges in contacting eligible patients. Resident trainees perceived having PN in their ambulatory practice to be beneficial.

Clinical Practice of Referring Physicians Utilizing Open Access Endoscopy at Boston Medical Center

Anand Singla, MD

Open access endoscopy (OAE) is defined as the performance of endoscopic procedures by referring physicians without prior clinic consultation. Traditionally, physicians have requested consultations for their patients by a GI endoscopist to determine whether endoscopic intervention was indicated. However, OAE has become increasingly used in both the US and Europe, including here at Boston Medical Center (BMC), making the referring physician responsible for management of antiplatelet agents and antibiotics prior to endoscopy. We sought to assess the clinical practice of physicians here at BMC who refer patients for gastrointestinal endoscopic procedures via OAE.

Methods: We conducted an online survey study of physicians here at Boston Medical Center who refer patients for gastrointestinal endoscopic procedures via OAE. Physicians included faculty in General Internal Medicine (GIM) and Family Medicine, as well as categorical residents in internal medicine and family medicine. Gastroenterologists here Boston Medical Center were also surveyed. The survey included three question series designed to assess clinical practice of antibiotic prophylaxis and management of antiplatelet agents prior to screening colonoscopy and EGD. General demographic information was also captured.

Results: A total of 280 invitations to participate in the survey were sent, out of which there were 212 responses, for a total response rate of 76%. Out of the 212 responses, a majority were residents or attendings in internal medicine. 136 were residents (64%) and 70 were attendings (33%). 126 (59%) felt they were unfamiliar with the current practice guidelines regarding the use of antibiotics and antiplatelet agents prior to gastrointestinal endoscopic procedures. There was significant variation in responses to questions regarding antibiotic prophylaxis in patients with prior history of endocarditis, mechanical aortic valve, vascular graft, hip replacement, and rheumatic heart disease.

Conclusions: Our findings indicate considerable variation in clinical practice among referring physicians who utilize OAE in regards to the use of antibiotics and antiplatelet agents prior to gastrointestinal endoscopic procedures. OAE raises important issues when it comes to familiarity with current practice guidelines among referring physicians. More work is needed to assess the effects of this practice variability on gastrointestinal endoscopic outcomes.

The Thyroid and Pregnancy: Regional Practice Pattern, Pavani Srimatkandada
Mentor: Dr. Elizabeth Pearce

Introduction: There is growing evidence of the impact of thyroid hypofunction on pregnancy and pregnancy outcomes. However, specific recommendations are controversial regarding thyroid function testing and the management of subclinical hypothyroidism and hypothyroxinemia during pregnancy. Current guidelines are often conflicting and there remains a lack of randomized clinical trial data. Insight into current practice patterns and opinions among medical professionals who care for pregnant women will allow for a better understanding of current patient care and of how existing guidelines are being implemented.

Methods: A multiple-choice questionnaire was compiled to assess demographic information and practice patterns in different regions. Questions aimed to determine how health care providers are approaching and managing thyroid health in pregnancy, and how these approaches differ across health care providers and regions of the United States. This survey was distributed at the annual American Thyroid Association meeting in September 2012. Questions were derived based on current management options in the field of thyroid management in pregnancy. Basic demographic information (professional degree, specialty, years or professional experience) was ascertained. The information from the survey was entered into an Excel spreadsheet. Primary analysis describes practice patterns regarding thyroid function testing and subclinical hypothyroidism and hypothyroxinemia in pregnancy. The frequency of each answer was assessed to determine practice patterns and these practice patterns were compared across different demographics (e.g duration of practice, type of practice, rural/urban/suburban location) using ANOVA.

Results: 150 participants completed the survey. Subject population consisted of American Thyroid Association members. The majority 91% of surveys were completed by endocrinologists, 0.65% by obstetric/gynecologist, 2.6% by general surgeons. 40% of practitioners saw between 1-10 pregnant women, 23% saw 11-20 pregnant women and 16% saw over 40 pregnant women in their practice annually. 73% percent of participants believed in screening all pregnant women while 18% felt that not all pregnant women should be screened and 8% were unsure. Over 75% of participants read the ATA guidelines while 68% read the Endocrine Society guidelines. There was no correlation between the decision for routine testing and those who read the ATA guidelines. However, those who read the Endocrine Society guidelines were more likely to test. Results indicate that those in an academic setting are less likely to favor universal testing compared to private single specialty practices. Also those who practice more than 20 years were more likely to order tests than those currently in training. Discrepancies existed in some data. For instance there appeared to be no difference in opinion regarding universal testing based on whether or not participants read the ATA guidelines. Item 11 of the questionnaire posed the scenario of a healthy pregnant woman without any thyroid risk factors. Preliminary data shows that those who read the ATA guidelines were less likely to favor testing in this scenario.

Conclusion: The majority of data indicates no significant predictors to indicate who was more likely to test versus those who were not. Weaknesses of the study included the low power of the study and the lack of variability in the background of participants. The majority of participants were Endocrinologists but even within the Endocrine community there exists conflicting practice patterns.

Role Of A Human Long Non-Coding RNAs In Lung Tumorigenesis

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Background: Improved understanding of the molecular changes associated with lung cancer progression is needed. The discovery that 90% of the genome is transcribed into non-coding RNAs (ncRNAs) has initiated a new era in the gene regulation field. Long non-coding RNAs (lncRNAs) have been identified as key players in epigenetic regulation. Aberrant lncRNA function may drive tumorigenesis through disruption of normal cell processes. Microarray studies have already identified increased expression of the antisense lncRNA *NKX2-1 AS* in cigarette exposure and lung cancer. Given the physiological importance of normal *NKX2-1* mRNA expression levels in lung development and its dysregulation in disease, and the similar alterations in expression patterns of the *NKX2-1 AS* and *NKX2-1* in lung disease, it is important to evaluate the functional roles of *NKX2-1 AS* in regulating expression of *NKX2-1* and other target genes in lung cancer progression, including tumor cell migration and invasion.

Methods: To evaluate the function of *NKX2-1AS*, cell lines were transfected with siRNA targeting *NKX2-1AS* and changes in cell shape and cell growth curves were measured. We also evaluated the effect of silencing *NKX2-1AS* on expression of neighboring genes by qRT-PCR and microarray analysis.

Results: In human lung cancer cell lines, *NKX2-1AS* and *NKX2-1* mRNA expression positively correlate. *NKX2-1*mRNA is down-regulated in human H441 lung cells transfected with siRNA targeting *NKX2-1 AS*, suggesting that *NKX2-1 AS* works to control the expression of *NKX2-1*. Silencing *NKX2-1 AS* in human lung epithelial cells alters cell shape to a fibroblast-like morphology with loss of cell-cell attachments and reduces cell proliferation at 72 hours. Two key genes altered in *NKX2-1AS* knockdown cells, specifically *MEGF10* and *TNS4*, were validated by qRT-PCR at different time points. *MEGF10* was confirmed to be upregulated at 72 hours while *TNS4* was found to be downregulated at 72 hours.

Conclusions: The similar expression pattern of *NKX2-1AS* and *NKX2-1* mRNA in human lung cells suggests a role of this lncRNA in regulating *NKX2-1* mRNA. Since increased expression of *NKX2-1AS* in lung cancer and reduction of *NKX2-1AS* expression by siRNA show changes in cell shape and cell growth, *NKX2-1AS* may serve as a critical drug target in lung tumorigenesis. *NKX2-1 AS* appears to play an important role in regulating both *NKX2-1* and other genes in lung cancer cells.

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Mentor: Kalpana Gupta, MD

Title: A Rare Complication of BCG Immunotherapy for Bladder Cancer

Case Description: RC is a 64 year old male Vietnam veteran with bladder cancer s/p recent completion of intravesicular BCG therapy who presented to the West Roxbury VA Hospital complaining of 2 weeks of fevers, nausea/vomiting, and altered mental status. Symptoms developed immediately after his last BCG administration. ROS was notable for a 30 pound weight loss over the past year. Physical examination was notable for orthostatic hypotension and tangential thinking, but was otherwise unremarkable. Laboratory investigation revealed pancytopenia, acute kidney injury, and hypercalcemia with a corrected value of 13.8. PTH was in the low/normal range; Vit D 1,25 OH and ACE levels were elevated. Vit D 25-OH was normal. Calcium normalized and renal function improved after aggressive administration of normal saline, pamidronate, and calcitonin. While in house, RC developed dyspnea and required supplemental oxygen. A chest CT showed diffuse, bilateral reticular-nodular opacities and a right pleural effusion. At this point, differential diagnosis included a hypersensitivity reaction to BCG, disseminated BCG or *M. Bovis* infection, and sarcoidosis. Bronchoscopy yielded negative AFB BAL, smear, and culture; TST and quantiferon testing were also negative. Bone marrow biopsy yielded a negative AFB smear and no evidence of granulomas. Repeat CT showed large bilateral pleural effusions and resolution of reticulonodular opacities. He was diuresed with improvement in respiratory status and discharged on furosemide. Six weeks later, RC was re-admitted from renal clinic with recurrence of acute kidney injury and hypercalcemia after restarting Vitamin D supplementation. He also had an elevated alkaline phosphatase at 433 with elevated GGT. RUQ ultrasound demonstrated no evidence of cholelithiasis or abnormal liver parenchyma with possible liver hemangioma. RC was discharged after IVF and pamidronate administration. Four weeks later, RC was re-admitted again with hypercalcemia and acute kidney injury. Liver biopsy showed granulomatous hepatitis. He was started on prednisone, INH, and rifampin with resultant resolution of hypercalcemia, improvement in renal function, and normalization of liver function tests.

Discussion: BCG immunotherapy is usually safe since most complications are mild: cystitis and dysuria (80%), hematuria (40%), and fever (30%). In less than 1% of patients, serious side effects can occur either locally (granulomatous prostatitis, retroperitoneal abscesses) or systemically (sepsis, pneumonitis, hepatitis, hypersensitivity syndromes). The case of Mr. C demonstrates a rare, but serious complication of BCG therapy: disseminated *M. bovis* infection causing multiorgan disease. BCG infections can be categorized as 'early presentation' or 'late presentation' disease. The former occurs within 3 months of BCG instillation, often has hypersensitivity features, and in nearly every case, involvement of liver and lungs. Biopsies reveal granulomas and mycobacteria are rarely recovered in cultures. Late presentation disease often occurs greater than 1 year after treatment initial BCG treatment and usually involves focal disease of the genitourinary tract and/or retroperitoneal tissues. Granulomas are often present and mycobacteria are more likely isolated. Similarly to most patients, RC responded well to antituberculous therapy and corticosteroids.

L1CAM Expression correlates with Metastatic Spread on Endoscopic Ultrasound – Guided – Fine – Needle Aspiration of Pancreatic Cancers

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Background: Pancreatic cancers carry a poor prognosis and represent the 4th leading cause of cancer deaths in the United States. At time of diagnosis these cancers may already have lymph node involvement or metastatic spread, precluding the possibility of curative surgery and ensuring a poorer prognosis. The 5-year survival rate of resectable pancreatic cancer is approximately 20% compared to less than 5% in unresectable cancers. L1 cell adhesion molecule (L1CAM) is a transmembrane glycoprotein that is not expressed in normal pancreas, but its expression in surgically-resected pancreatic cancers has been shown to correlate with prognosis, lymph node involvement, and metastatic disease. Prognostic markers of pancreatic cancer found before surgical resection with endoscopic ultrasound-guided-fine -needle aspiration (EUS-FNA) may guide patient treatment. This study aims to explore the clinical significance of L1CAM in pancreatic cancers diagnosed by EUS-FNA.

Methods: Pathology specimens from 13 consecutive patients diagnosed with pancreatic cancer by EUS-FNA between 2010-2011 were retrieved for immunohistochemical staining of L1CAM (Abcam, Cambridge, MA) through retrospective review of patient electronic medical records. Records were re-examined at the end of 2011 to confirm that these diagnoses were correct. The immunostain of formalin-fixed, paraffin-embedded tissues was performed according to recommendations by the L1CAM antibody manufacturer, including overnight incubation at a 1:50 dilution at 4°C, final development with 3,3' diaminobenzidine substrate (Abcam), and counterstain using hematoxylin (Sigma-Aldrich, St. Louis, MO). Appropriate positive and negative controls were conducted simultaneously. Once stained, the slides were scored by a blinded experienced gastrointestinal pathologist. Expression was considered when immunoreactivity of neoplastic cells was detected in over 10% of the total number of estimated neoplastic cells. The clinical course of each patient was retrospectively examined for lymph node involvement and presence of metastasis detected by imaging, endoscopy, or surgery performed within one month from time of initial diagnosis.

Results: L1CAM expression was identified in 5 patients and absent in 8 patients. At time of diagnosis 3 patients with L1CAM expression had lymph node involvement and 4 had metastatic spread. All 5 patients had either lymph node involvement or metastasis. In the group with absent L1CAM expression no patients had lymph node involvement and only 1 patient had metastasis.

Conclusion: L1CAM expression in pancreatic cancers diagnosed by EUS-FNA correlates with lymph node involvement and metastasis at the time of diagnosis, and may serve as a clinical prognosticator. Future large prospective studies are warranted to evaluate L1CAM's role in management of pancreatic cancers.

An easily overlooked cause of dyspnea and weight loss

David Wholey, PGY-3

A 55 y/o male presented to primary care clinic for evaluation of weight loss. He reported 20 pounds of unintentional weight loss over the prior six months in addition to three months of intermittent dry cough and mild exertional dyspnea. He had a history of COPD, pulmonary sarcoidosis, and nonischemic cardiomyopathy. He used a regimen of tiotropium, budesonide, salmeterol, and albuterol for respiratory symptoms. He had a 25 pack year smoking history but quit 5 years previously. He was born in Alabama and had travelled there recently, but denied any other travel. He had never been incarcerated or homeless.

Results: On physical exam revealed a thin, comfortable-appearing male. He was afebrile with normal vital signs. Pulmonary examination showed no accessory muscle use, symmetric chest expansion without deformity, and distant breath sounds with scattered expiratory wheezes. Cardiovascular examination revealed normal S1 and S2 without murmurs or gallops, jugular venous pressure was not elevated, and no peripheral edema was present. Laboratory tests included angiotensin converting enzyme level 36 U/L (range 9-67) and 1-25 dihydroxy vitamin D level 58 pg/mL (range 18-72). HIV ELISA testing was negative.

Chest X-ray noted flattened hemidiaphragms bilaterally, calcified hilar and mediastinal lymphadenopathy, and multiple bilateral upper lobe nodular opacities. CT scan of the chest further characterized the nodules as multifocal with upper lobe predominance (largest 3.8 cm with a speculated appearance), which were new from his last imaging study 5 years earlier. PET/CT demonstrated FDG-avidity of multiple mediastinal and supraclavicular nodes. Spirometry revealed a mild airflow obstruction with slightly increased lung volumes and mildly low DLCO, without significant change from a prior study the year prior.

Bronchoscopy was performed with grossly unremarkable airways. Brushings taken that were negative for malignancy. Bronchoalveolar lavage cytology was negative for malignancy. Mycobacterial cultures returned positive for mycobacterium avium complex after 12 days.

Discussion: The patient's respiratory symptoms were attributed to pulmonary mycobacterium avium infection after malignancy and active pulmonary sarcoidosis were ruled out. He was began on a regimen of azithromycin, rifampin, and ethambutol with a planned 12 month course once negative sputum cultures were achieved. At follow up visit 2 months after initiating treatment the patient's weight had stabilized and he reported significant improvement in respiratory symptoms. Three month follow up chest CT demonstrated a stable appearance of pulmonary nodules and lymphadenopathy.

Conclusion: Mycobacterium avium complex (including M. avium and M. intracellulare) is a free-living organism that is ubiquitous in the environment and can be pathogenic in the immunocompromised or patients with pre-existing structural lung disease. Diagnosis can be missed due to the subacute and non-specific nature of the symptoms as well as variable radiographic findings (including infiltrates, nodules, and cavitary lesions), both of which are frequently masked by the underlying lung pathology. Diagnosis requires microbiological identification of the causative organism in addition to compatible respiratory symptoms and radiographic findings.

Identification of Medication Reconciliation process inefficiencies at a community health center

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Objective: Several studies have shown that medication discrepancies reported in the ambulatory setting range from 25-75%. These medication errors account for more than 7,000 deaths annually and \$3.5 billion in hospital costs. In order to improve patient safety across the continuum of care, the performance and accuracy of patient medication reconciliations conducted by providers in an ambulatory setting at a community health center in Boston was examined. The main objective of the project was to identify and determine the root causes of the inefficiencies in the medication reconciliation process.

Methods: Lean management tools were utilized to map the outpatient medication reconciliation process, identify inefficiencies in the process and construct a fishbone diagram to determine root causes of the inefficiencies.

Results: A process map was developed and through systems thinking with stakeholders the following areas of inefficiencies were identified: length of patient waiting time prior to the physician encounter and the need for a decision to be made by the provider regarding performing a medication reconciliation at the end of the encounter. By implementing a simple standardized reconciliation form involving the key stakeholders ensured that medication reconciliation would be systematically addressed during each patient-physician encounter without adding significant time or additional steps to the total encounter.

Conclusions: Lean management rooted in synergistic efforts by health care workers and patients is essential in identifying inefficiencies and solutions to improving the medication reconciliation process in an ambulatory setting. Piloting this intervention at a community health center and assessing the associated patient outcomes need to be further studied and measured against our proposed metrics of success.

Intensive Peri-Discharge Intervention Reduces 30-Day Readmissions in an Underserved Heart Failure Population: Demonstration of a Validated Risk Score

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Background: We developed and validated in an underserved population a 30-day readmission risk score consisting of 3 factors available at the time of admission for heart failure (HF) (HF admission in the prior month, systolic blood pressure (SBP) ≤ 125 mmHg, and eGFR < 45 ml/min/1.73m²). No studies have investigated the applicability of a risk score model in assessing the efficacy of an intervention at reducing hospital readmissions, particularly in a demographically vulnerable population.

Hypothesis: We tested the hypothesis that an intensive, peri-discharge intervention will reduce 30-day all-cause readmissions as compared to 1) standard care patients and 2) risk score-predicted readmissions.

Methods and Results: The study population consisted of 654 patients admitted to Boston Medical Center for HF from May 2010 to June 2011. Nearly 70% were black or Hispanic and 80% received public insurance. The Intervention group (n=130) received a peri-discharge intervention consisting of intensive education prior to discharge, telephone contact at 1-3 days, and an outpatient visit with a nurse practitioner at 5-10 days post-discharge. The remaining patients (n=524) received Standard Care. Of the 138 patients readmitted within 30 days of discharge, 120 (22.9%) were in Standard Care vs. 18 (13.7%) in the Intervention group (OR=0.54 [0.31-0.92], p = 0.02). The effect of the intervention was unchanged by adjustment for age, SBP, and hemoglobin. Predicted readmission rates based on the risk score were similar in the Standard Care (25.8%) and Intervention groups (26.5%). A significant reduction (vs. predicted) was observed in the Intervention group (p = 0.01) but not the Standard Care group (p = 0.13).

Conclusions: In an underserved patient HF population, an intensive, peri-discharge intervention reduces 30-day readmissions. Our previously validated risk score model is a useful tool to identify patients at high risk of readmission.