End of Life (EOL) Planning has been a recent subject of ardent debate in the political arena. Media coverage on “death panels” has focused on patient skepticism surrounding the true objectives of end of life care planning. An investigational study aimed at developing a patient centered End of Life Care Planning Protocol at Chatham Crossing Medical Center (CCMC), a University of North Carolina Hospitals (UNCH) affiliated community based primary care practice, was designed. The project proposal was submitted to the local Institutional Review Board (IRB) and deemed to not require IRB approval.

Review of 147 patient encounters from visits completed within a one week period of time, with representation from all attending physicians based in the practice, revealed that 0% (0/147) had documentation of advanced directive discussion in the dictated clinic note from the encounter. 0.01% (1/147) had a completed note in the Advanced Directives section of the electronic medical record (EMR).

32% of patient charts reviewed (47/147) had documented hospitalization noted in the electronic medical record within the last 8 years. Of these patients, 47% (22/47) had no code status documented in the admitting physician’s History and Physical. 40% of patients (19/47) had full code status documented. 4% (2/47) had documented Do Not Resuscitate/ Do Not Intubate (DNR/ DNI) code status documented. The remaining 11% of hospitalizations (4/47) were hospitalizations outside the UNCH system; admission History and Physical notes from these encounters were not accessible for review.

Subsequently, 25 clinic patients were interviewed regarding their opinions about approach to EOL planning discussions. When asked about the timing of physician initiated end of life care planning discussions, 68% (17/25) patients felt the conversation should occur now or should have occurred in the past. 8% 2/25 did not know when they would like such a conversation to occur; 8% of patients wished to have this conversation when functionally or medically declining; 4% (1/25) wished to have such a conversation when diagnosed with an imminently terminal condition. 12% (3/25) did not comment.

In order to understand physician perspectives on initiating End of Life Care Planning discussions with patients, fourteen providers were interviewed from the UNCH system, with 11 providers from CCMC. When asked when a physician would ideally initiate EOL discussions, 79% (11/14) stated that they would like to initiate such discussions at the initial patient encounter or early in their relationship with the patient. 21% (3/14) felt that such discussions should occur in the setting of patient decline. Barriers to initiating discussions include time, lack of understanding about the patient’s wishes, fear of being misunderstood by the patient, and perceived lack of expertise in conducting effective discussions.

As a part of ongoing clinic quality improvement efforts, a Plan Do Study Act (PDSA) cycle providing patients with EOL planning questionnaires during annual visits at CCMC will be implemented in the summer of 2010. Patient responses will be entered into the EMR by nursing staff. Patient will be encouraged in the questionnaire to discuss any areas of concern with their physician. Follow up surveys evaluating patient and physician satisfaction with the process, as well as chart review looking at percentage of Advanced Directive EMR documentation will be conducted.

In summary, patients and physicians are unified in their desire to proactively address EOL planning. There remains a discrepancy between patient and physician ideals and actual practice with respect to EOL planning, in both inpatient and outpatient settings. Interventions making such discussions more systematic and streamlined will be studied in order to bring ideal practice goals closer to actual practice.
Thymic carcinoma and agranulocytosis

Thymic carcinoma is a rare disease that represents less than 1% of thymic neoplasias. Fifty to sixty percent of thymic neoplasias develop a paraneoplastic syndrome. The most common is myasthenia gravis, however pure red cell aplasia occurs in 5-15%, and more rarely pure white cell aplasia with hypogammaglobulinemia in less than 5%. Thymic carcinoma is more aggressive and typically presents with cough, dyspnea, chest pain, phrenic nerve palsy, or symptoms of a paraneoplastic syndrome. In our case, a 73 year old male was admitted to the hospital with a 1 week history of dysphagia, diarrhea and cough. He was transferred for further care from an outside hospital where he had been diagnosed with a urinary tract infection, leukopenia, and a concern for mediastinal mass on chest radiograph. On arrival to the hospital he was found to have esophagitis, white blood count of 0.4 (ANC 0.0 and ANL 0.3), and was short of breath. A CT scan performed showed a 6.6 x 4.4 cm necrotic anterior mediastinal mass. A bone marrow biopsy on hospital day 2 was performed revealing hypocellular bone marrow with granulocytic aplasia. On day 5 of hospitalization, a biopsy of the mass was performed and identified thymic carcinoma. The patient was started on cyclophosamide and prednisone therapy, as well as radiation therapy, as he was not a candidate for surgical resection.
Correlation Between VerifyNow Assay and CYP2C19 Polymorphisms

Michael Cammarata, MD; Jaya Dharmavaram, MD; George Stouffer, MD PhD; Joseph Rossi, MD

BACKGROUND: Clopidogrel and aspirin combination therapy are standard of care in patients status post PCI. Even with optimal treatment, thrombotic events occur, partially due to clopidogrel resistance and novel CYP2C19 loss of function mutations. Screening for these mutations is currently expensive or not known to be reliable. Our aim is to find an inexpensive point of care test which can reliably discern patients more likely to have the mutation.

METHODS: 32 stable CAD patients were screened and had simultaneous VerifyNow platelet assay and genetic testing. The data from the various genotypes were then analyzed using the unequal variance T-test method against wild type genotype.

RESULTS: There was a non-significant trend toward increased platelet reactivity among the CYP2C19*2 heterozygotes compared to wild-type (P=0.11).

CONCLUSION: Preliminary findings suggest a trend towards decreased platelet inhibition among CYP2C19*2 loss of function heterozygotes. After enrollment of the target 200 patient sample a more complete analysis can be completed.

Department of Medicine, Department of Radiology, Division of Cardiology, UNC Chapel Hill

Background

Patients presenting to an acute care facility with chest pain or dyspnea often undergo multiple radiologic evaluations in the process of pursuing a diagnosis, ruling out dangerous conditions, and stratifying risk. However, there is little information on the amount of radiation exposure accrued in the evaluation of chest pain and dyspnea. Our objective was to determine the type and number of radiologic tests used in the evaluation of chest pain or dyspnea at UNC, and estimate the amount of radiation exposure.

Methods

A retrospective review of patients older than 18 years of age presenting to the UNC Emergency Department from March 1, 2008 to April 30, 2008, with the chief complaint of chest pain or dyspnea was performed (excluding STEMI). Radiologic tests, labs, and history performed in the ED, inpatient setting, or in the 3 months after presentation related to the chief complaint were included. Effective dose of radiation for each type of study at UNC was calculated by UNC physicists and used to calculate estimated radiation exposure for each patient.

Results

476 patients were studied, with 20% younger than 40 years old, 27% with a history of CAD. Overall, 88 nuclear cardiac perfusion studies, 63 CT/PE scans, 15 CT dissection scans, 14 V/Q scans, 11 CT coronary angiography scans, and 75 cardiac catheterizations were performed. Overall, the final diagnosis was noncardiac chest pain in 50% of the patients, while acute coronary syndrome occurred in 35 patients (7%), stable angina in 13 (3%), PE in 6 (1%), and aortic dissection in 1 (0.2%). The most common other diagnoses made were pneumonia (38 patients, 8%), CHF exacerbation (37 patients, 8%), and COPD exacerbation (30 patients, 6%).

15 patients underwent multiple advanced radiologic studies (most commonly a CT/PE protocol scan, and a cardiac nuclear perfusion study), and 36 patients received over 25 mSv of total radiation in their workup, with one patient receiving 42 mSv in a single evaluation. The majority of patients undergoing a CT/PE protocol scan did not receive an initial D-dimer.

Conclusions

There is significant radiation exposure in the evaluation of chest pain or dyspnea. Use of radiologic tests was significant in young persons, and even in young females. There are multiple opportunities to reduce radiation exposure. First, we should use non-radiologic tests where appropriate, based on pre-test probabilities and test performance. Examples include initial D-dimer in evaluation of PE, use of stress EKG or TTE instead of nuclear perfusion studies, and MRI for aortic dissection or coronary perfusion. Second, education of these principles for physicians, especially emergency physicians, may be beneficial as they are the first contact and order many of the radiologic studies. Finally, development of a single test that can evaluate multiple disease states, such as the CT triple scan for evaluation of CAD, PE, and dissection could reduce redundant tests. A significant weakness of our study is underestimation of total radiation exposure, as we are only studying presentations and tests within UNC, and tests only relating to the evaluation of chest pain and dyspnea.
Abstract 1:

While patients with functional GI disorders (FGIDs) are managed as outpatients, a proportion are hospitalized for diagnostic evaluation and treatment. We sought to determine: (1) the prevalence and clinical features of inpatients with FGID diagnoses seen on the gastroenterology (GI) consultation service; and (2) the value of diagnostic testing. We found that patients with FGIDs seen by the GI consult service at a teaching hospital had frequent prior healthcare visits and also had many diagnostic studies that continued during their current hospitalization. However, the utility of repeated testing is questionable for existing FGID symptoms; only if objective clinical features change should repeat testing be considered.

Abstract 2:

Little is known about the reasons patients in tertiary care teaching hospitals are referred for in-patient gastroenterology consultations and the diagnoses they ultimately receive. Therefore, we sought to determine the requesting in-patient service and the reasons for in-patient gastroenterology consultations. Among GI consultations seen in a one-year period at a tertiary care teaching hospital, the majority were requested for GI hemorrhage, IBD, and functional GI symptoms/disorders. Narcotic bowel syndrome is an emerging clinical entity. It needs to be determined whether these findings are similar to other inpatient GI settings.
Title: Prognostic Value of Immune Cell Function Assay on Biopsy Results and Infection in Cardiac Transplant Patients

Ria D Dancel, MD, (rdancel@unch.unc.edu)\(^1\), Chris Wiesen, PhD, (Chris_Wiesen@unc.edu)\(^1\). Patricia P. Chang, MD, (patricia_chang@med.unc.edu)\(^1\). \(^1\)University of North Carolina, Chapel Hill, NC, United States, 27713.

Purpose: One previous study suggested that heart transplant patients with strong immune cell response (measured by the Cylex ImmuKnow assay) were at higher risk of rejection, whereas patients with low immune cell response were at higher risk of infection (ideal levels: 225-525 ng/mL ATP in CD4 cells); other studies could not replicate this finding. The purpose of this study is to correlate levels of intracellular ATP in CD4 cells with episodes of acute rejection or infection in heart transplant patients followed at UNC Hospitals (UNCH).

Methods and Materials: We conducted a retrospective review of adult heart transplant recipients at UNCH who had Immuknow assay results and associated heart biopsy and culture results between September 2006 and September 2009. Acute cellular rejection was defined as ISHLT grade ≥ 2R. Infection was defined as presence of positive pathogen in blood, sputum, or urine cultures. Differences in Immuknow levels over time between groups were assessed using a mixed effects model.

Results: Among 114 patients (77 men, 37 women; mean age 44.8 ± 19.6 years at transplant) with 602 Immuknow levels (5.3 ± 4.6 levels per subject), there were 26 episodes of rejection, 64 infections (27 bacterial, 17 viral, 5 fungal, 15 mixed), and 9 combined rejection and infection episodes, during a mean follow-up period of 6.5 ± 4.9 years post-transplant. Mean Immuknow levels over time in patients with rejection (281 ± 29 ng/mL), bacterial (342 ± 32 ng/mL), viral (317 ± 36 ng/mL), or fungal (204 ± 56 ng/mL) infection were not different from levels in patients who did not have these events (302 ± 7 ng/mL) (all p=NS). The high intraclass correlation (38%) suggested high inter-subject variability.

Conclusions: Immuknow levels between patients were widely variable and not associated with acute rejection or infection, refuting the idea that set ranges of intracellular ATP in CD4 cells are predictive of rejection or infection. Whether this assay can track a patient’s immune response on an individual level needs further study.
Prinzmetal’s Angina after chemotherapy: 5-FU as a cause of coronary vasospasm
Scott Haake, MD and Paul Johnson, MD
Department of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC.

The presentation of a patient with chest pain and ST-segment elevations on EKG most often represents occlusion of a coronary artery with clot, and subsequent myocardial infarction. However, not all chest pain with EKG changes represents acute coronary syndrome. Medication effects are rarely associated with this presentation but must be considered if no coronary disease is identified, as specific treatment is required for resolution of symptoms.

A 62 year old woman with Stage I chronic kidney disease, hypertension, and newly diagnosed Stage IIIB appendiceal adenocarcinoma treated with 5-fluorouricil (5-FU) and leucovorin infusion two days prior to presentation came to the ER one hour after the onset crushing, substernal chest pain, bilateral hand numbness, and shortness of breath. EKG on arrival demonstrated ST-segment elevations in leads I, aVL, V1, and V2. She underwent emergent coronary angiography which demonstrated normal coronary anatomy without obstructing lesions. A V/Q scan showed no evidence of pulmonary embolism. Creatinine kinase (CK) and MB fraction of creatinine kinase (CKMB) were within normal limits, but troponin-I was slightly elevated at 0.049 ng/mL (upper limit of normal 0.034 ng/mL). Her EKG normalized after angiography. That evening, however, she had a repeated episode of chest pain, again demonstrating ST-segment elevations on EKG. Her chest pain and EKG changes resolved after administration of sublingual nitroglycerin. Isosorbide mononitrate 30 mg daily and diltiazem SA 240 mg daily were started. Her symptoms improved and EKG failed to show evidence of evolving infarction. Her troponin-I peaked a 0.099 ng/mL on day of presentation, with CK and CKMB remaining normal. A transthoracic echocardiogram showed preserved LV systolic function. She was subsequently discharged home free of chest pain. One week later she was seen in follow up with her oncologist, and the shared decision was made to discontinue further 5-FU treatments.

Coronary artery vasospasm, also know as variant or Prinzmetal’s angina, can present with substernal chest pain and transient ST-elevations on EKG. While commonly thought to arise from autonomic nervous system and endothelial dysfunction, medications have also been reported to cause vasospasm. 5-FU, an anti-metabolite that acts during S phase of the cell cycle, is a known cardiotoxin that has been associated with myocardial infarction, ventricular arrhythmias, and cardiac arrest. While the biochemical mechanism of cardiotoxicity from 5-FU is still unclear, it is thought to be mediated through coronary vasospasm. Our patient’s clinical course would support this hypothesis. This case demonstrates that it is critical to identify all potential causes of coronary vasospasm in order to appropriately treat and prevent further adverse outcomes.
Venous thromboembolism in malignant gliomas.

Malignant gliomas are associated with a very high risk of venous thromboembolism (VTE). While many clinical risk factors have previously been described in brain tumor patients, the risk of VTE associated with newer anti-angiogenic therapies such as bevacizumab in these patients remains unclear. When VTE occurs in this patient population, concern regarding the potential for intracranial hemorrhage complicates management decisions regarding anticoagulation, and these patients have a worse prognosis than their VTE-free counterparts. Risk stratification models identifying patients at high risk of developing VTE along with predictive plasma biomarkers may guide the selection of eligible patients for primary prevention with pharmacologic thromboprophylaxis. Recent studies exploring disordered coagulation, such as increased expression of tissue factor (TF), and tumorigenic molecular signaling may help to explain the increased risk of VTE in patients with malignant gliomas.
**Prolonged hypoglycemia after insulin glargine overdose**

Paul Johnson, MD and Benjamin Vincent, MD  
Department of Internal Medicine  
University of North Carolina, Chapel Hill, NC

**Introduction**

The widespread availability and use of insulin, along with its capacity to induce severe hypoglycemia and coma, make this drug a dangerous agent in suicide attempts. Surprisingly, there are relatively few case reports of suicide by insulin overdose in the literature. We describe a case of suicide attempt by injection of 2,000 units of insulin glargine and 500 units of insulin aspart, and the prolonged hypoglycemia that followed.

**Case Description**

A 38-year-old female with a history of Type II diabetes mellitus, obesity, and depression presented to the emergency department 20 minutes after taking 2,000 units of insulin glargine and 500 units of insulin aspart. She was diaphoretic and nauseated, but mentating well at presentation. Her blood glucose on arrival was 42 mg/dL. She was given 25 grams of IV dextrose and a D10W infusion at 100 ml/hour was started after central line placement. Her glucose levels were routinely monitored every 30 minutes and during periods of symptomatic hypoglycemia. Despite the continuous dextrose infusion, she had 16 recorded episodes of glucose levels below 60 mg/dL, requiring bolus infusions of dextrose.

Her blood glucose did not return to baseline until the fourth day in the ICU. The D10W infusion was stopped and glucose monitoring extended to two-hour intervals. The patient was transferred to the psychiatry floor on the sixth hospital day. Her blood glucose remained in the normal range despite withholding insulin. On hospital day eight, her blood glucose began to rise above 200 mg/dL, and 10 units of subcutaneous insulin glargine were given and up-titrated to 20 units each night before discharge on hospital day 10.

**Discussion**

Insulin glargine is a peak-less insulin analogue with a protracted effect of 20 to 24 hours. The absorption rate decreases with increasing dose when administered subcutaneously. Hypoglycemia can occur rapidly in overdoses and the risk of continued hypoglycemia may extend for many hours past the expected duration of drug action. This case illustrates the need for prolonged intensive care monitoring in patients who overdose with long-acting insulin. Our patient required a continuous dextrose infusion for 138 hours, longer than any previous case reported in the literature thus far. While management of insulin overdose is not complicated, the consequences of unrecognized hypoglycemia are severe, and frequent blood glucose monitoring is warranted.
Treatment of Pneumonia due to Metapneumovirus in an immune competent patient with IV Ribavarin
Kidd JM, Hall WB and Aris RM

Metapneumovirus (hMPV) was first described in 2001 in a case series of children in the Netherlands. (van den Hoogen et al 2001) It is a single stranded RNA virus in the Paramyxoviridae family. hMPV has been associated with respiratory tract infections in all age groups. Most published reports in the adult literature have been associated with elderly and immune compromised patients.

We present a case of an otherwise healthy 59 year old female who developed left lower lobe pneumonia and hypoxic respiratory failure associated with a positive hMPV viral swab requiring admission to the intensive care unit. She was treated with a 5 day course of Ribavarin and was discharged from the hospital. Human metapneumovirus is an emerging pathogen in the adult population and further study into possible treatments is warranted. In our estimation, this is the first reported case of an immunocompetent individual with respiratory failure from hMPV and successful outcome with Ribavarin therapy.

Reference:
van den Hoogen BG, de Jong JC, Groen J, Kuiken T, de Groot R, Fouchier RA and Osterhaus AD 2001
A newly discovered human pneumovirus isolated from young children with respiratory tract disease; Nat Med. 7 719-724
An Elusive Rash in an Alcoholic: A case report

Joseph J BHSc¹, McWilliams A MD², Kolappa, K MD³, Buzan A MD*.

Case Presentation

A 45 year old male with a history of alcohol abuse presented to the emergency department with a diffuse, scaly, and intensely pruritic rash. The rash, which was photosensitive, started on his upper extremities and spread proximally to involve his trunk and lower extremities. The patient underwent multiple visits to emergency departments and to a dermatology clinic for evaluation of this rash. He was first diagnosed with scabies and prescribed antihistamines and topical steroids, though none of his close contacts had similar symptoms. During the next few months, he developed lower extremity edema with progression of the rash. At this time, he returned to his dermatologist, and the worsening rash was felt to be medication induced. He continued to be treated for apparent scabies. Four months following his initial diagnosis of scabies, the patient presented to the emergency department in acute renal failure with a creatinine of 9.16 and was admitted. He was cachetic and dehydrated with a diffuse macular, erythematous and scaling rash of the bilateral upper and lower extremities, abdomen and lower back as seen in Figure 1. A closer examination of the patient's history revealed 6 months of emesis, abdominal pain, dysgeusia, intermittent dysphagia, a 30 pound weight loss, diarrhea, short-term memory loss and visual hallucinations involving parasites crawling out of his skin. The patient also admitted to drinking 18 to 24 alcoholic beverages daily for several years. His nutritional status was further compromised by the emesis and dysgeusia. An endoscopy revealed erosive esophagitis and duodenitis consistent with mucosal inflammation. An echocardiogram was obtained for concern of high output cardiomyopathy secondary to thiamine deficiency but was unremarkable. He was also screened for C. Difficile infection and heavy metal toxicity, which were both negative. The patient was aggressively rehydrated with intravenous fluids, given vitamin supplementation, and placed on a calorie-restricted diet, while being monitored closely for re-feeding syndrome.

During the hospitalization, his kidney function gradually normalized, cognition improved, and the rash regressed significantly. The patient's dysgeusia, dysphagia, and gastrointestinal symptoms also improved to the degree that he was able to tolerate a low calorie diet while maintaining stable laboratory values and vital signs. One week later, his nausea, vomiting, and diarrhea returned. He became anemic, oliguric and hypoxic on room air. Chest plain films revealed bilateral airspace consolidation consistent with ARDS and he was started on broad-spectrum antibiotics. His hypoxia worsened and he was subsequently intubated. Over the next few days, he developed septic shock becoming hypothermic with a leukocytosis and hypotension requiring multiple vasopressors. Despite aggressive resuscitative therapy, he progressed to renal failure with worsening acidosis and fulminant liver failure evidenced by hypoalbuminemia, thrombocytopenia and coagulopathy. Ultimately, his family decided to transition to comfort care.

Conclusion

This case is presented to illustrate that pellagra, a treatable disease when diagnosed early, can present atypically and result in complications including death if diagnosis is delayed.
Background: Randomized clinical trials have failed to show a mortality benefit of drug-eluting stents (DES) in the setting of acute coronary syndrome (ACS) despite markedly reduced rates of restenosis. Elderly patients have been underrepresented in most large clinical trials comparing DES to bare metal stents (BMS).

Methods: Analysis of Medicare Provider Analysis and Review files from 2003 and 2004 identified 180,672 PCI procedures among beneficiaries >65 years admitted with ACS using discharge diagnosis and procedure codes. We developed a logistic regression model for outcomes incorporating demographics (including Medicaid buy-in, zip-code level median household income, and rurality as categorized by Rural Urban Commuting Area), and patient comorbidities. End points were assessed separately for the STEMI and NSTEMI/UA population and included death, recurrent ACS and repeat revascularization.

Results: Mean age was 76.0 years, 51% were male. DES was alone was used in 49.2% of cases. STEMI diagnosis codes were identified in 27.9%. At baseline, DES patients were younger, had increased incidence of diabetes and were less likely to have a history of CHF, stroke or chronic lung disease. After adjustment for demographic variables, comorbidites, and community level variables, DES use was associated with a decreased risk of mortality at 3 years compared to BMS for patients with STEMI (OR 0.72, 95% CI 0.68-0.76, p<0.001) and non-STEMI/UA diagnoses (OR 0.76, 95% CI 0.74-0.80, p <0.001). For a combined endpoint of death, MI, or repeat revascularization, DES was again associated with a significant reduction in endpoints at 3 years for STEMI (OR 0.71, 95% CI 0.66-0.75, p <0.001) and non-STEMI/UA (OR, 0.80, 95% CI 0.77-0.84, p-value<0.001).

Conclusions: Among elderly patients admitted with ACS, DES use is associated with decreased mortality and decreased composite endpoint of death, MI, and repeat revascularization compared to BMS. It is possible that BMS selects for patients with a poor prognosis, and unmeasured variables account for the difference noted here. However, these results suggest a possible benefit of DES among elderly patients with ACS.
Focal adhesion kinase regulation affects proliferation in both neonatal cardiomyocytes as well as pathologic remodeling.

O'Neill TJ, DiMichele LA, Doherty JT, Rojas M, Beggs HE, Reichardt LF, Mack CP, Taylor JM.

The cardiomyocyte phenotypic switch from proliferative to anabolic growth is crucial both for normal heart development and pathologic myocardial remodeling observed during the progression to dilated cardiomyopathy. This switch is due, in part, to the action of focal adhesion kinase (FAK) a protein activated following integrin-mediated interactions with the extracellular matrix. Indeed, studies from our lab and others indicate that FAK is essential for cardiac morphogenesis. FAK activity can be dynamically regulated by expression of its endogenous dominant negative interfering mutant, termed FAK related non-kinase (FRNK) and we recently found that FRNK is dramatically upregulated in neonatal hearts during the transition from proliferative to anabolic growth. To define a role for FAK-FRNK interactions in myocardial growth, we first created an transgenic mouse where FRNK was constitutively expressed in hearts from mid-gestation onwards (rather that only transiently postnatally) which led to embryonic lethality and cardiac noncompaction associated with decreased myocyte proliferation. In contrast, a second transgenic mouse which induced persistent FRNK expression in post-natal hearts onwards did not affect anabolic heart growth or function but impaired hypertrophic response to overload. To determine whether FRNK acted in a cell autonomous fashion to regulate myocyte proliferation, we measured the proliferation of cultured cardiomyocytes infected with FRNK adenovirus or a control vector. The FRNK infected cells had reduced proliferation and increased p38 phosphorylation. Finally, we measured expression of p38-dependent cell cycle regulating proteins in wild type and FRNK knockout hearts. In FRNK -/- hearts the cell cycle entry inhibitors p21, p27 and p53 as well as cdc42 were each decreased at post-natal day 10 compared to wild type mice. In combination these findings suggest a role for FRNK mediated suppression of cardiomyocyte proliferation in developmental (and perhaps adult) settings. This represents a potential therapeutic avenue in settings where additional proliferation would be desired such as post-infarct necrosis and dilated cardiomyopathy.
Using Electronic Decision Support to Expand Access to Care in South Africa

Loren Robinson, MD, Marc Mitchell, MD, Neal Lesh

Background: In sub-Saharan Africa, the acute shortage of physicians and nurses severely limits the rollout of HIV care and treatment. This problem has become particularly acute as the numbers of AIDS patients on anti-retroviral (ARV) therapy has increased since these patients are, fortunately, now living longer and need routine care for indefinite periods of time. In low income areas, where patient burden is high and doctor shortage is common, future expansion of AIDS treatment will occur in rural clinics with the majority of patient visits being managed by non-physician medical personnel. We have developed and evaluated a PDA-based tool to guide lay counselor staff step-by-step through screening algorithms in order to support task-shifting.

Objective: To evaluate whether lay counselors using screening protocols on a PDA can accurately determine which patients need referral to a physician during routine HIV treatment visits.

Methods: The trial was conducted at the Tygerberg and Helen Joseph Hospitals in South Africa and included adult patients on ARVs for at least 3 months during routine monthly visits. Participants first met with a counselor using a PDA running software we developed that presents a series of assessment questions derived from the Integrated Management of Adult Illness (IMAI) protocols. Participants then saw a doctor who provided care and filled out a form indicating any medical problems. The PDA results were compared with these forms for specificity and sensitivity.

Results: Of 715 patient encounters at both hospitals collected during an 18 month period 298 had some medical problem requiring referral. Of these, 214 were correctly identified by the PDA based on clinical symptoms, and an additional 53 were referred on the basis of factors available in the patient record, such as a high viral load. Of the remaining 30 false negatives, only 4 were identified as serious enough problems that their doctors would have recalled the patient before their next visit had they left the clinic without treatment. Of the 417 encounters not requiring referral according to the doctor, 234 were correctly identified by the PDA leaving 183 false positives. Of these, 40 cases included genital problems or use of traditional medicines which the doctors admitted they often overlook.

Discussion: Given the shortage of physicians in Africa, it is imperative to shift patient care to less skilled health workers. Lessons learned from the deployment of the PDA program included increased clinical knowledge of the adherence counselors, added workload and clinic space requirements, and the need for a clinician or counselor designated as the PDA coordinator for each site, so that site-specific staffing, clinic flow, and technical issues can be addressed as they arise. While further refinement of the questions are necessary, the use of electronic job aids can play a key role in addressing the bottleneck of the lack of a trained health workforce for scaling up HIV care and treatment. This study suggests that electronic job aids can correctly triage most patients on ARVs, thereby reducing the need for physician care.
Variable Effects of Combination Corticosteroids and Catecholamines on Total β2-Adrenergic Receptors in Human CD4+ T-Lymphocytes

Rationale: Studies show that β2-adrenergic receptors (β2AR) on human peripheral blood mononuclear cells (PBMC) are associated with immune deviation (ID) of the adaptive immune response towards a T-helper 2 (TH2) phenotype. Recent data suggest that these effects are increased when adrenergic agents (AA) are coincubated with corticosteroids (CS) in vitro. We therefore examined the effects of combination CS and AA on total β2AR expression in human CD4+ T-lymphocytes using a novel flow cytometry assay to investigate a potential mechanism of ID. Methods: PBMC from normal human subjects (n=7) were stimulated with PHA and were incubated with stress-physiologic concentrations of epinephrine (EPI), dexamethasone (DEX), or the combination of both hormones. Changes in the mean fluorescence intensity (MFI) of β2AR were measured by flow cytometry (FC).

Results: β2AR MFI significantly decreased in the presence of EPI at 10^-6 (9.77 ± 0.10), 10^-7 (10.18 ± 0.15), and 10^-8 (9.78 ± 0.16) or DEX (9.48 ± 0.18) at 10^-8 Molar (M) when compared to control (12.61 ± 0.36, p<0.001). The combination of EPI at 10^-8 and DEX at 10^-8 M (12.67 ± 0.48) did not significantly differ from control (p>0.05).

Conclusions: The data show that AA and CS at various stress-physiologic concentrations significantly decreased the total cellular content of β2AR in CD4+ T-lymphocytes. However, no effect was observed when both hormones were incubated together.
Encouraging the Use of Wells Criteria in Risk Stratifying Pts with Presenting Symptoms Concerning for Pulmonary Embolism
Kristine Scruggs, MD; Allen Liles, MD

Background: Pulmonary embolism (PE) can result in significant morbidity and mortality if not diagnosed and treated early. Research has shown that physicians do not consistently use clinical assessment tools, such as the Wells criteria, to determine pretest probability of PE before ordering CT angiography. There is increasing data to show that radiation and IV contrast exposure leads to future health concerns, such as kidney failure and radiation-induced malignancy. Incomplete assessment of PTP also results in effectively decreasing the positive predictive value of the CTA, resulting in a higher number of false positive results. Likewise, if PTP is high but not assessed, a negative CTA result is falsely reassuring. Even the use of D-dimer alone without first calculating a patient’s PTP is not supported in the literature; this practice can result in a missed diagnosis of VTE in upwards of 9% of the population. The use of a clinical assessment tool in combination with D-dimer measurement has been shown to safely exclude the diagnosis of pulmonary embolism in 46% of patients presenting to the ED in whom PE is suspected.

Methods: A cohort of patients who received and were billed for a CTA during 11/2009 for the purpose of diagnosing PE was examined. A chart review was performed to evaluate the use of PTP calculation and D-dimer prior to CTA. At the same time, an attempt was made to estimate the Wells score from retrospective chart review. Information regarding performing service and clinical setting was also obtained.

Results: At UNC, physicians who ordered CT scans for the purpose of “ruling out” pulmonary embolism mentioned a clinical pre-test probability in 8/112 cases (7.1%). Of these, some were based on clinical “gestalt” rather than an actual calculation. Physicians were correct in their clinical assessment of PTP in only 4/112 cases (3.6%). In patients with a low PTP (Wells score <2), D-dimer was checked in 24/58 (41.4%). In patients with an “unlikely” PTP (Wells score <= 4), D-dimer was checked in only 28/88 (31.8%). By extrapolating data from Wells et al, CTA could potentially have been avoided in favor of less invasive, costly, and inconvenient studies in 40/112 patients (36%). In outpatients (those presenting to clinic or to the ED), 61/74 patients (82.4%) had Wells scores of <= 4, making their clinical probability for PE “unlikely.” Only 22/61 with “unlikely” PTP had D-dimers measured. Again, extrapolating from research performed by Wells et al, 28/74 patients may have been effectively “ruled out” for PE without any further testing. Incidence of PE in this cohort of patients (with CTA used as the gold standard) was 11.6%. This is lower than the typical 20% incidence in previous studies examining the performance of CTA in detecting PE, thus negatively affecting the PPV.

Conclusions: Pulmonary embolism is a fairly common and potentially fatal diagnosis if not managed appropriately and in a timely manner. Many diagnostic studies have been shown to aid in diagnosis of PE, but efficacy is proven in the setting of routine pretest probability assessment. Many clinicians forego PTP tools in favor of radiologic studies (specifically, CTA) likely because of convenience, the desire to obtain other information from the studies, and general confidence in the quality of the study. However, the performance of CTA decreases if used inappropriately in a population of patients who have not been appropriately assessed for their PTP of PE. Studies have shown that providing clinicians with tools such as posters, pocket cards, or handheld devices to assist with decision making results in more appropriate use of testing and a higher comfort level in discontinuing the work-up when enough information has been obtained. A similar system could likely be utilized at UNC by providing a desk-top application or posters with an algorithm that is easy to follow and approved to be used hospital-wide.