GW RESEARCH DAYS 2012
MARCH 28 & 29

THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON DC
17th Annual Health & Medicine Research Day

Wednesday, March 28, 2012

Marvin Center – 800 21st Street, NW

8:00 – 9:00 A.M.
Posters to be Mounted on Posterboards

Media and Public Affairs Building – 805 21st Street, NW

8:00 – 9:00 A.M.
Registration and Breakfast

9:00 – 9:05 A.M.
Welcome & Introduction of Keynote Address
Jeffrey S. Akman, M.D.
Interim Vice President for Health Affairs and Dean, School of Medicine and Health Sciences

9:10 – 10:00 a.m.
Keynote Address
Lisa M. Guay-Woodford, M.D.
Director, Clinical and Translational Science Institute at Children’s National Medical Center (CTSI-CN)
Associate Vice President for Clinical and Translational Research, The George Washington University
“Polycystic Kidney Disease: A Paradigm for Translation Research and its Clinical Impact”

10:05 – 10:55 a.m.
Keynote Address
Paula Lantz, Ph.D.
Chair, Department of Health Policy, School of Public Health and Health Services
“Improving Population Health Through Community-Based and Policy Translational Research”

10:05 – 10:55 a.m.
Introduction of Keynote Speaker
Lynn Goldman, M.D.
Dean, School of Public Health and Health Services

10:55 – 11:15 a.m.
Coffee Break

11:15 a.m. – 12:00 p.m.
Panel Discussion: “Translational Research Across the Continuum”
MODERATOR: Vincent A. Chiappinelli, Ph.D.
Interim Associate Vice Provost for Health Affairs and Associate Dean, School of Medicine and Health Sciences
Lisa M. Guay-Woodford, M.D.
Paula Lantz, Ph.D.
Marlene Lee, RN, MSN
Nurse Manager, General Clinical Research Center, CNMC
Henry Kaminski, M.D.
Meta Amalia Neumann Professor and Chair of Neurology, School of Medicine and Health Sciences

12:30 – 2:00 p.m.
Distribution of Box Lunches (Rooms 301 and 302)

12:30 – 3:00 p.m.
Poster Session and Judging
(Grand and Continental Ballrooms, 3rd Floor)

Marvin Center – 800 21st Street, NW

3:00 – 4:00 p.m.
Poster Removal

3:00 – 4:30 p.m.
Award Ceremony (includes 10-minute presentations by winners of oral competition awards from each School) (Room 403)
AWARD CEREMONY

3:00 – 4:30 P.M.

SCHOOL OF MEDICINE AND HEALTH SCIENCES
Moderator: Vincent A. Chiappinelli, Ph.D.
Interim Associate Vice Provost for Health Affairs and Associate
Dean, School of Medicine and Health Sciences
Bradley T. Anderson – “Radiosensitization of Melanoma Cell Lines
Using the Mutant B-Raf Inhibitor GSK2118436”

INSTITUTE OF BIOMEDICAL SCIENCES
Moderator: Linda Werling, Ph.D.
Associate Dean for Graduate Education, School of Medicine and
Health Sciences; Director, Institute of Biomedical Sciences
Kristin Ceniccola – “The glucagon receptor functions as a tumor
suppressor that is lost in advanced-stage hepatocellular carcinoma”

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES
Moderator: Lynn R. Goldman, M.D., M.S., M.P.H.
Dean, School of Public Health and Health Services
Christel Host – “Time trends in diarrhea mortality in Mexican
children under 5: the population effect of various interventions
including water, sanitation, and the rotavirus vaccine”

HEALTH SCIENCES
Moderator: Mary Corcoran
Professor of Clinical Management and Leadership
Samar A. Nasser, Ph.D., M.P.H., PA-C – “Effect of
Dimethylarginine Dimethylaminohydrolase in the Development
of Salt Sensitivity”

SCHOOL OF NURSING
Moderator: Ellen Dawson, Ph.D.
Senior Associate Dean, School of Nursing
Lamin Juwara – “Compassion Fatigue among Oncology Nurses”

RESIDENT ORAL PRESENTATION
Moderator: W. Scott Schroth, M.D., M.P.H.
Associate Dean for Administration, School of Medicine
and Health Sciences
Dr. Matthew Wallac, PGY4, Resident in Orthopedic Surgery

2012 DORIS DEFORD SPECK AND GEORGE SPECK, M.D.
ENDOWED PRIZE
Moderator: Vincent A. Chiappinelli, Ph.D.
Zachary Ashwell – “The Epidemiology of Mountain Bike Park
Injuries at the Whistler Bike Park, British Columbia”

2011 ELAINE H. SNYDER CANCER RESEARCH AWARD
Presenter: Vincent A. Chiappinelli, Ph.D.
Rakesh Kumar, Ph.D.
Professor and Catharine Birch and William McCormick Chair,
Department of Biochemistry
Jeanny Aragon-Ching, M.D.
Assistant Professor, Department of Medicine

2012 DISTINGUISHED RESEARCHER AWARD
Presenter: Vincent A. Chiappinelli, Ph.D.
John N. Van Den Ankler, M.D., Ph.D.
Professor of Pediatrics and Pharmacology and Physiology
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CHARACTERISTICS OF METHICILLIN-RESISTANT AND METHICILLIN-SUSCEPTIBLE STAPHYLOCOCCUS AUREUS STRAINS FROM PATIENTS WITH COMMUNITY-ACQUIRED PURULENT SKIN AND SOFT TISSUE INFECTIONS IN WASHINGTON, DC

BACKGROUND

Staphylococcus aureus is responsible for >50% of all Emergency Department (ED) outpatient skin and soft tissue infections (SSTI). Many of these community acquired strains have unique combinations of resistance traits and virulence factors. It is important that healthcare providers understand the characteristic trends of S. aureus infection within their local communities in order to provide appropriate treatment.

OBJECTIVES

To describe 1) the clinical and demographic characteristics of an urban population presenting with SSTI and 2) the molecular typing characteristics of S. aureus isolates.

METHODS

Consenting subjects (≥18 years old) who presented to an urban ED with purulent SSTI and received abscess incision and drainage were enrolled in this ongoing, IRB approved study. A swab of the wound site was sent to the clinical laboratory for culture and antimicrobial susceptibility testing. S. aureus isolates were further characterized by S. aureus Protein A (spa) sequence typing and PCR detection of the methicillin resistance genes (SCCmec and mecA) and the Panton-Valentine Leukocidin (PVL) toxin gene (LukF-PV and LukS-PV).

RESULTS

72 subjects have been enrolled, of which 50% are male, 80.5% are Black and 30.5% have significant comorbidities (Diabetes, HIV, IDU, Other). S. aureus was isolated from 39 (54%) subjects, of which 72% were MRSA and 28% were MSSA. Spa type t008 was responsible for 50% of the S. aureus infections. PVL toxin gene was present in 100% of the MRSA and 55% of the MSSA isolates; no difference in 48 hour outcome between PVL(+) and PVL(-) infections was observed.

CONCLUSIONS

This study revealed data similar to previous findings in a DC population. Healthcare workers should be aware of these strain characteristics to provide appropriate treatment. Ongoing surveillance of community acquired S. aureus is important to detect emerging strains.
K-ras codon 12 GGT to GAT mutation is not elevated in the duodenum of mice subchronically exposed to hexavalent chromium in drinking water

Chronic exposure to high concentrations of hexavalent chromium [Cr(VI)] in drinking water induces small intestinal tumors in mice, but the mode of action (MOA) for carcinogenicity is uncertain and could be informed by assessing Cr(VI)’s genotoxicity and mutagenicity in the target tissue of the duodenal epithelium under conditions of the cancer bioassay. Thus, binding of Cr to genomic DNA, and K-ras codon 12 GAT mutation frequency were evaluated in intestinal epithelium of B6C3F1 mice exposed to sodium dichromate dihydrate (0.3-520 mg/L) in drinking water for 7 and 90 days. Cr-DNA binding increased in a time- and concentration-dependent manner, reaching statistical significance at higher concentrations (≥ 14 mg/L). Cr-DNA binding in the non-target tissues of the liver and oral mucosa was also significantly increased, and in the liver measured at levels consistent with that of the duodenal epithelium at carcinogenic doses. These findings suggest that Cr-DNA binding may be a biomarker of exposure. The frequency of K-ras codon 12 GAT mutations was analyzed using allele-specific competitive-blocker PCR (ACB-PCR) and by Sanger sequencing of codons 12 and 13. K-ras mutant fraction (MF) in duodenal epithelium was not increased with dose. Moreover, it was approximately 100-fold greater than expected (10-2 to 10-3), which may suggest that this tissue is susceptible to neoplasia via a cytotoxicity/regeneration MOA. The lack of Cr(VI)-induced K-ras codon 12 GAT mutation at carcinogenic doses suggests induction of this mutation through Cr-DNA binding, or otherwise, is not an early key event in the MOA of Cr(VI)-induced duodenal carcinogenesis.
Background

In medical imaging literature, geometric registration is an unsolved problem that has been intensively investigated. It can be used to match two scans obtained from different imaging modalities. Iterative closest point algorithm (ICP) has been widely used for surfaces or range scans registration. ICP calculates the rigid transformation between two surfaces by minimizing the Euclidean distance of the correspondent point pairs. This distance-based measure can lead to local minima. The use of anatomical landmarks can improve the registration accuracy. Manual landmark selection can cause localization error, and intra- and inter-observer variations. ICP requires searching all the points of a surface to determine the best correspondence of another surface point with O(n^2) time complexity.

Methods

A novel non-rigid registration method that registers two deformable surfaces by using the cover tree for the correspondence computation of ICP. The aim is to find the correct correspondence without landmark selection and to reduce the computational complexity. Our method consists of: initial alignment, cover tree construction, piecewise rigid (p-rigid) ICP, and non-rigid ICP steps. Cover tree is constructed by considering the positions and normal vectors of the points. In p-rigid ICP, the two surfaces are divided into clusters by applying cover tree-based clustering and the source is deformed closer to the target by transforming each of its clusters to its corresponding cluster on the target. In non-rigid ICP, the source is deformed to the target by determining the correct corresponding point pairs between two surfaces and optimizing a proposed energy function. Candidate correspondences are determined by searching the neighborhood of a given source point from the cover tree and the best correspondence is found by estimating a correspondence measure, including the Euclidean distance and local geometric similarity. The proposed correspondence measure helps to find the correspondence with more similar geometric features by considering the angular difference and connectivity. The proposed energy function, which consists of the fitting term, smoothness term, and Jacobian penalty term, accurately deforms the surface with less deformation folding.

Results to Date

Experimental results for different CT and Kinect surfaces show that our method led to the best result in terms of the visual inspection, clustering cost, registration time, and registration accuracy.

Conclusions

Proposed method for non-rigid registration is marker-less and reduces the time from O(n^2) to O(n*((1-c)^4*d)/(1-(c)^4)) in p-rigid ICP and to O(c^12 * n *log n) in non-rigid ICP.
A Variant in the Supervillin Gene is Associated with Lean Muscle and Adiposity Phenotypes

BACKGROUND

Supervillin is a 205-kD F-actin binding protein encoded by the SVIL gene that is described as a linkage protein between the actin cytoskeleton and plasma membrane in a variety of cell types. The protein potentially functions in cellular adhesion, as well as muscle development and repair as a co-regulator of androgen receptor gene transcription. Similarly, SVIL may also influence vitamin D receptor functioning and associated bone health through androgen receptor signaling. Our study sought to further describe the relationship between the SVIL gene and phenotypes associated with lean muscle, bone, and adipose tissue by examining single nucleotide polymorphisms (SNPs) that may have a functional relationship to the SVIL gene.

METHODS

We studied 155 ethnically diverse, healthy volunteers (average age 22.05 ± 4.82 yrs females and 23.31 ± 5.61 yrs males) recruited from the Bone and Muscle Study performed at the University of Massachusetts. We genotyped two SNPs found in SVIL (rs36027845 and rs10437410), and examined associations between these variants and measures of lean muscle tissue, bone mineral density, and adiposity. Mean quantitative muscle, bone, and adipose measurements were compared in relation to SNP genotypes using analysis of covariance (ANCOVA) methods.

RESULTS

1) In male subjects, single copy of the G allele for a SNP located near the SVIL gene (rs36027845) was associated with decreased total lean muscle mass (p = 0.0157) and total arm lean muscle mass (p = 0.0295), as well as increased total percent tissue fat (p = 0.0190) and total fat (p = 0.0175). 2) No significant associations were determined in female subjects. 3) No significant findings were identified between the genetic variants of interest and phenotypes associated with bone. 4) No statistically significant relationships were identified for the rs10437410 SNP.

CONCLUSIONS

Significant associations were found between a variant in the SVIL gene (rs36027845) and decreased total and arm lean muscle mass, as well as increased percent tissue fat and total body fat in males. These results provide evidence indicating that the SVIL gene may play a role in the regulation of skeletal muscle development via co-regulation of the androgen receptor. An inverse relationship between skeletal muscle and adipose tissue was observed in males with the genetic variant, indicating that the polymorphism may also be associated with an increased risk for adiposity. Further study is warranted to elucidate the function of the SVIL gene in skeletal muscle development and implications in disease processes of the musculoskeletal system.
Background

The expression of the Id4 protein in a previous study has been shown to be restricted to a few cells lining the basement membrane of cross-sectioned murine seminiferous tubules, lending it to be a potential marker for Spermatogonial Stem Cells (SSCs). The following research strives to replicate the staining and results in a human model. A novel G Protein receptor, GPR125, has been shown in human models to be expressed in “1 or 2” cells lining the basement membrane of the seminiferous tubule cross sections, linking it also to being a marker for SSCs. This research also seeks to replicate these results.

Methods

Mounted slides of human cadaveric donor testes were warmed and run through a series of xylenes and alcohols. Antigen retrieval buffer was then added and the samples were steamed. An endogenous peroxidase block was then added. The primary antibody was added and the samples were incubated overnight at 4 degrees C. Secondary antibody was then added, then Streptavidin Horseradish Peroxidase, followed by an AEC substrate for slide development.

Results

Abnova Mouse Polyclonal Anti-Id4 Antibody yielded pale, diffuse, non-specific background with no clear staining of cells after several protocol alterations. Calbiotech Rabbit Monoclonal anti-Id4 showed several darkly staining nuclei per cross section of seminiferous tubule of all 16 patients, around 12 to 30 nuclei stained per cross section.

With GPR-125, similar manipulations of protocol were altered as with the Id4 protocol. Out of the many antibodies tested, Novus Goat Polyclonal anti-GPR-125 antibody showed almost every cell lining the cross-sectioned sample to express the protein in a ring-like fashion, sparing the nucleus. There was, however, a considerable background staining the entire seminiferous tubule cross-section. Sigma anti-GPR showed similar results with less clarity.

Conclusions

Expression of Id4 in human testes models was limited to nuclei of cells lining the basement membrane of the seminiferous tubules with an average of 12 to 30 nuclei per cross section. There was also possible staining of Sertoli cells. These nuclei were likely from cells of undifferentiated spermatogonia, but not necessarily limited to only SSCs. With GPR-125, considerably more than the ”1 or 2” cells on the basement membrane per cross section were stained with anti-GPR-125 antibody, making it also unlikely to be a marker for SSCs.
Targeting Treatment to the Neuromuscular Junction: Advancing Therapy for Myasthenia Gravis

Myasthenia gravis is a devastating autoimmune, neuromuscular disorder caused by antibodies, which activate complement-mediated damage of the post-synaptic surface of the neuromuscular junction. Present treatments may be ineffective and uniformly have significant adverse effects which lead to a poor quality of life. The goal is to better define the role of complement in myasthenia gravis pathogenesis and to target complement inhibitors to the neuromuscular junction as a therapeutic approach. Our primary hypothesis is that targeting a complement inhibitor to the neuromuscular junction will be the ideal therapeutic agent for myasthenia gravis by (1) concentrating complement inhibition to the site of pathology at the neuromuscular junction, (2) extending the half-life of the compound, and (3) limiting toxicity of systemic complement inhibition. A single chain antibody directed against the alpha subunit of the acetylcholine receptor was synthesized (designated scFv-35) and coupled to the complement inhibitory domains of the decay accelerating factor (scFv-35-DAF). We have evaluated the agent’s ability to concentrate to the NMJ and its potential therapeutic effect in experiment MG (EAMG) in mice and rats. We administered scFv-35-DAF to mice deficient in intrinsic complement inhibitors, which are highly susceptible to EAMG. The mice were found to gain weight and exhibited no loss of strength indicating the construct did not inhibit NMJ transmission. The scFv was found to localize to the NMJ and there is no evidence of tissue destruction in the complement regulator deficient mice. We also administered scFV-35-DAF to Lewis rats and induced EAMG. The rats treated with scFv35 developed severe weakness within 24 hrs, while scFv-35-DAF rats developed moderate weakness. We demonstrate for the first time a method to target a therapeutic to the NMJ. The ultimate goal is produce the first drug specifically designed for treatment of myasthenia gravis.
Background

Submucosal glandular (SMG) hyperplasia is a primary histopathologic feature in obstructive respiratory pathologies associated with mucus hypersecretion, such as chronic rhinosinusitis and cystic fibrosis. Glandular hyperplasia in respiratory tract mucosa is markedly understudied, reflecting the lack of an in vitro model whereby respiratory tract epithelial cells differentiate into glandular cells. The current paradigm is that basal cells (BCs) function as progenitor cells in the respiratory tract epithelium, poised to facilitate epithelial repair and remodeling. We hypothesize that BCs differentiate to form glands in a 3D extracellular matrix and are triggered by inflammatory/immune response mediators and growth factors to produce glandular hyperplasia in disease conditions. To test this hypothesis, we developed an in vitro 3D system wherein BCs from primary epithelial cells differentiate into glandular structures when grown on different basement membrane matrices.

Methods

Human airway epithelial BCs were assessed with immunofluorescence staining (IF) using BC specific markers (cytokeratin 5, P63, and Integrin α6) and fluorescence-activated cell sorting (FACS). BCs from human nasal epithelial (HNE) and sinus epithelial (HSE) cells were differentiated on Matrigel® and collagen 1 (COL1) for 20 days. Glandular mucous and serous markers were detected by immunostaining and confocal microscopy. HNE BCs were exposed to different doses of epidermal growth factor (EGF), fibroblast growth factors (FGF7 and 9) and inflammatory mediators (CXCL5, CXCL13, GM-CSF, IL6 and IL8). The average surface area of acini and growth kinetics were compared before and after exposure to mediators by bright field microscopy.

Results

FACS analysis of purified HNE cells and human bronchial epithelial (HBE) cells indicated that 98% of cells were BCs and BCs markers were expressed in >95% of cells on IF staining. The morphological differentiation of BCs in in vitro culture is dependent upon extracellular matrix conditions. While BCs differentiate into glandular acini when overlaid on Matrigel®, they differentiate into glandular tubules when embedded in collagen. Both glandular acini and tubules formed by HNE cells in vitro expressed in vivo markers of mucous and serous glandular cells. Exposure of HNE basal cells to EGF, FGF7 and FGF9 enhanced their proliferation rate, suggesting that growth factors may play an important role as positive regulators of the morphogenesis and differentiation of submucosal glands in respiratory tract mucosa. Although statistically significant, the increased HNE acinar size seen after exposure to inflammatory mediators (CXCL5, CXCL13, and GM-CSF) was small.

Conclusions

The in vitro 3D glandular system is a useful model for evaluating the effects of growth factors and other mediators on proliferation and differentiation of HNE and HSE cells into SMG and potentially useful for studies of glandular proliferation and hyperplasia in disease states.
Global DNA Methylation Changes in Brain Tissues from Individuals with Autism

BACKGROUND

Although epigenetic changes have been proposed to play a role in the etiology of autism, there has been no study to date which has investigated global methylation changes in the brain of individuals with autism.

OBJECTIVE

The goal of this study was to identify differentially methylated genes in brain samples from individuals with autism that may be relevant to the neuropathology of autism. To accomplish this, we performed global methylation profiling of post-mortem tissues from the frontal cortex (BA9/10) and cerebellum of 7 and 8 male individuals with autism, respectively, and compared the methylation profiles with that of age- and sex-matched controls.

METHODS

Genomic DNA was extracted from the brain tissues and enriched for methylated regions was isolated using Epigentek’s Methylamp Methylated DNA Capture (MeDIP) Kit. Affymetrix Human Promoter 1.0R GeneChips were used to analyze differentially methylated promoter regions in the enriched DNA (normalized by input DNA). Partek GS 6.6 beta software was used to analyze the intensities across the promoter regions using the workflow for methylation analyses. Significantly differentially methylated genes were subjected to functional and pathway analyses using Ingenuity Pathway Analysis (IPA) network prediction software.

RESULTS

Over 4000 promoter elements representing over 2000 unique genes were found to be differentially methylated in both frontal cortex and cerebellum of individuals with autism relative to the age-matched controls. There was an overlap of 754 differentially methylated genes between the two brain regions, including a number of previously identified autism candidate genes. Pathway analysis of these overlapping genes showed significant enrichment in genes involved in axon guidance, melatonin signaling, semaphorin signaling, and synaptic long-term potentiation. Application of Pavlidis template matching to the respective sets of differentially methylated genes further reduced the set of genes to 63 cortical and 96 cerebellar genes whose methylation profiles completely separated cases from controls. Among these genes, S-phase kinase-associated protein 2 (SKP2) was found to be differentially methylated in both the frontal cortex and cerebellum. SKP2 is thus identified as a novel autism susceptibility gene, which has been shown to be essential for the proliferation and differentiation of neuronal precursor cells.

CONCLUSIONS

Our results show global changes in the brain methylome of individuals with autism relative to that of age-matched controls. The differentially methylated genes in the frontal cortex and cerebellum are involved in pathways that are known to be disrupted in autism.
GW MEDICAL FACULTY ASSOCIATES

Exploring the Effect of Relaxation Interventions to Reduce Anxiety, Depression and Pain, and Improve Sleep and Medical Outcomes Among Hemodialysis Patients

BACKGROUND

Dialysis is a necessary treatment for thousands of people with kidney disease, most of whom also suffer from high levels of anxiety, depression, pain and sleep deprivation. In addition, many of these patients do not adhere to their dialysis treatment, which can threaten their survival and quality of life. These physical, psychological and behavioral problems are particularly prominent among low-income African-American renal patients. This research examined the extent to which a low-cost, field-based audio PMR program can reduce anxiety, depression, pain, sleep deprivation and non-adherence among dialysis patients. Progressive muscle relaxation (PMR), has been shown to have powerful positive effects on anxiety, depression, pain and sleep. However, in most cases, PMR training has required one-on-one sessions with a therapist, followed by extensive practice at home. This can involve significant extra time and expense, which also may be burdensome, especially for low-income patients. By contrast, this intervention enables patients to conduct self-directed PMR training and practice (using audio CDs created for this purpose) during their dialysis sessions.

METHODS

Patients were screened for study eligibility via questionnaire. Those patients with greater than population-average anxiety or with sleep and pain ailments were randomly enrolled into an experimental group, PMR, or the placebo control, music. Patients enrolled in the audio intervention for six weeks, after which a post-test questionnaire was administered. Four weeks after completion of the program, a second post test was administered.

RESULTS

Nineteen patients on hemodialysis were enrolled (13 male, 6 female) into the experimental PMR group (n=10) and control Music group (n=9). Results will be available and discussed during the symposium.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Evaluation of the 10-Point Clock Drawing Test as a Screening Tool in Chronic Pain Patients

BACKGROUND

Cognitive dysfunction includes attention deficit; learning memory; speed of information processing and psychomotor ability; executive-type function. The incidence of cognitive dysfunction in the chronic pain population and the correlation with variables such as pain intensity is unclear. Cognitive studies typically include neuropsychological testing which can be time consuming. Cognitive skills necessary to complete the 10-point clock test include comprehension, planning, visual memory, visuo-spatial ability, motor programming and execution, numerical knowledge and abstract thinking. We hypothesize that this test can be useful screening tool for cognitive dysfunction in chronic pain patients.

METHODS

To perform the test, each patient is given a pre-drawn four-inch-diameter circle and asked to draw in the face of the clock followed by the time ten past eleven. To score it, a transparent circle divided into eighths is applied to the clock drawn. Points are given for each number falling into the appropriate segments (1, 2, 4, 5, 7, 8, 10, and 11) and one point is given for an obvious short hand pointing at 11 and a long hand pointing at 2. Cognitive impairment is unlikely with a score of 10, very likely with a score of eight and significant impairment is likely with a score less than five. We reviewed 45 charts from July 2011 to December 2011 of patients who were administered the 10-point clock drawing test in the GW Pain Center. We looked at the following variables: age; gender; race; BMI; pain diagnosis; duration of pain; pain score; pain interventions; opioid and non opioid use.

RESULTS

Of the 45 patients, 67% had a clock score of 8 or less (33% 9+). Of these patients, the average pain score (0-10) was 7.01 (6.6 for 9+). The higher pain scores concentrated around the groups with lowest clock scores. There were no significant correlations among other variables and the clock drawing test.

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CONCLUSION

Cognitive skills necessary to complete the 10-point clock include comprehension, planning, visual memory, visuo-spatial ability, motor programming and execution, numerical knowledge and abstract thinking. There appears to be a correlation between higher chronic pain scores and low clock drawing test scores. We were unable to correlate other variables to the 10-point clock drawing test. Prospective studies with a larger sample size may help further determine the use of the clock drawing test as a screening tool in the chronic pain population.

References


Qualitative Analysis of Thai Massage from the Perspective of the Thai Massage Practitioner

BACKGROUND

Traditional Thai massage is one of four branches of Traditional Thai medicine and involves accessing deep pressure points, stretching, and herbs. Traditional Thai massage is recognized and regulated by the Thai government as a therapeutic modality for mind and body, and is gaining popularity worldwide. This study evaluates the perspectives of Traditional Thai massage practitioners and their students, their perceived benefits of Thai massage and the reasons for providing it. In addition, it explores global perceptions of Thai massage and restrictions to practicing effectively in community settings.

METHODS

A total of 15 Thai massage practitioners from the Thai Massage School of Chiang Mai (TMC), Thai Massage Conservation Club Chiang Mai Branch 2, and international students training to be certified in Thai massage at TMC were interviewed using a 13 question survey. Interviews were recorded and transcribed. Collected data was analyzed using standard qualitative analysis methods. Those not proficient in English or without a bilingual translator present were excluded from the study.

RESULTS

The results showed a vast difference between Thai and international perspectives. Thai participants selected Thai massage as their sole profession because they enjoy providing massage, while non-Thai massage practitioners use Thai massage as an addition to services they provide. 50% of international participants chose to learn Thai massage because they view it as an energy healing and spiritual modality in addition to physical healing. 20% of participants mentioned that massaging over a clothed client was a favorable aspect of Traditional Thai massage. According to the Thai participants, traditional Thai massage is perceived as positive and therapeutic in their communities while 50% of international participants stated that it is misconceived as a sexual service in their communities. 83% of international participants stated that little is known about Traditional Thai massage in their community. As for most common treatment, responses varied evenly between shoulder and back pain, tension relief, and whole body relaxation. Restrictions include allopathic contraindications, lack of anatomical knowledge, and laws regarding massage practice where they reside. Overall, the dominant theme that was identified is that Traditional Thai massage is perceived more of a therapeutic modality rather than for relaxation.

CONCLUSION

Traditional Thai massage is an ancient healing art that is widely used as therapy in Thailand in conjunction with allopathic medicine. It is most commonly utilized by individuals experiencing headaches, musculoskeletal pain, and tension. While little is known about Traditional Thai massage in the western world, its reputation as a therapeutic and healing modality is gaining momentum.
Persistent changes in gene expression in ventral tegmental area of male and female adolescent rats treated prenatally with nicotine

Background
Although the health risks associated with smoking during pregnancy have been well established, it is estimated that 16.4% of women smoke during pregnancy. Many of these women use nicotine replacement therapy as an alternative to smoking. This has lead to a growing body of work concerning the childhood outcomes of prenatal nicotine exposure. Prenatal nicotine exposure is significantly associated with increased rates of nicotine addiction later in life, and increased difficulty in quitting. Our lab has previously compared effects of chronic nicotine exposure in adolescent and adult rats on gene expression in the ventral tegmental area (VTA), which consists of dopamine cell bodies that are a critical component of the reward pathway. Nicotine-induced changes in expression in adolescent rats were far more likely to persist for at least one month beyond the end of exposure than in adults, consistent with heightened brain plasticity during this period. We hypothesized that persistent changes would also exist in adolescents following prenatal nicotine exposure.

Methods
To test whether prenatal exposure altered gene expression in the VTA, we exposed fetal rats to saline or nicotine (6 mg/kg/day, free base) via osmotic minipumps planted subcutaneously in pregnant dams starting day 5 of pregnancy. Exposure continued throughout delivery, and pups continued receiving exposure through postnatal day 10 via mother’s milk. Male and female offspring were weaned at day 21, and sacrificed as adolescents at day 42, roughly one month after the end of nicotine exposure. Gene expression was measured using Affymetrix rat gene 1.0 ST microarrays. ANOVA treatment was performed with 10% FDR using Partek Genomics Suite. Network and gene ontology analysis was performed with Ingenuity Pathway Analysis.

Results
Numerous genes (>1000) in the VTA were found to be selectively and persistently altered by prenatal exposure. Many of the genes and canonical pathways that were altered differed between the male and female groups. Both groups showed differential regulation of serotonin receptors following prenatal exposure, although receptor subtypes affected differed by gender.

Conclusions
Prenatal exposure to nicotine caused changed levels of expression of a large number of genes in the VTA. These changes persisted at least one month beyond the end of drug exposure, into adolescence. Effects on gene expression differed widely in male and female offspring. Some of the genes affected may play a role in altered sensitivity to the effects of nicotine and other drugs of abuse in offspring of mothers who smoked while pregnant.
The histone deacetylase inhibitor trichostatin A downregulates expression of atrogenes in spinal muscular atrophy mice

**Background**

Muscle atrophy occurs in a variety of diseases and in specific muscles upon disuse or nerve injury. During atrophy, muscle protein is degraded through the ubiquitin proteasome pathway. In atrophy models, the E3 ligases atrogin-1 and MuRF1 are upregulated and mediate this protein degradation. Spinal muscular atrophy is an inherited neuromuscular disease characterized by motor neuron loss and muscle weakness. Histone deacetylase inhibitors such as trichostatin A improve body weight, life span, myofiber number, and area in a spinal muscular atrophy mouse model. As an HDAC inhibitor, trichostatin A may modulate atrogin-1 and MuRF expression in the muscle tissue of these mice.

**Methods**

SMA model mice and control littermates were treated with trichostatin A or vehicle from post-natal day 5 to 13. Muscle tissue was harvested for RNA or chromatin isolation. C2C12 muscle cell lines were treated with dexamethasone, trichostatin A or vehicle and collected for RNA isolation or protein degradation assays. C2C12 muscle cell lines were also transfected with atrogin-1 and MuRF1 reporter constructs, treated with trichostatin A or vehicle and assayed for luciferase expression.

**Results**

We show increased atrogin-1 and MuRF1 expression in the late stages of the disease in a spinal muscular atrophy mouse model. We provide evidence that myogenin mediates induction of atrogin-1 and MuRF1 in this mouse model and that trichostatin A can pharmacologically inhibit this upregulation.

**Conclusions**

Atrogin-1 and MuRF1 inhibition with trichostatin A treatment may contribute to the amelioration of the disease phenotype. While trichostatin A is a pan-HDAC inhibitor, more specific inhibitors of HDAC4/5 may improve the efficacy and reduce potential side effects. Importantly, modulating expression of critical genes in the atrophic pathway may represent a strategy for ameliorating atrophy in spinal muscular atrophy and other denervating diseases.
Identification of Transcriptional Targets of RORA, a Novel Candidate Gene for Autism Spectrum Disorder

BACKGROUND

We have recently identified the nuclear hormone receptor RORA (retinoic acid-related orphan receptor-alpha) as a novel candidate gene for autism spectrum disorder (ASD). Our independent cohort studies have consistently demonstrated the reduction of RORA transcript and/or protein levels in lymphoblastoid cell lines, the prefrontal cortex, and the cerebellum of individuals with ASD. Studies in mice have demonstrated that RORA is involved in ASD-related biological functions, including neuronal differentiation, cerebellar development, protection of neurons against oxidative stress, and regulation of circadian rhythm. However, little is known about the functions and transcriptional targets of RORA, particularly in human tissues.

OBJECTIVE

To comprehensively identify direct transcriptional targets of RORA in human neuronal cells using high-throughput whole-genome promoter analysis. Here we focus on RORA1 which is the major isoform of RORA in the brain.

METHODS

Formaldehyde-crosslinked chromatin was isolated from the human neuronal cell line SH-SY5Y and immunoprecipitated (IP) using anti-RORA1 or IgG antibody. DNA was purified from the IP chromatin and used for microarray analysis (ChIP-on-chip) using Affymetrix’s Genechip Human Promoter 1.0R Arrays, each of which comprises over 4.6 million probes tiled through over 25,500 human promoter regions. Probes significantly enriched in RORA1-IP DNA were identified using Partek software. Selected potential targets of RORA1 were then further validated by chromatin immunoprecipitation, followed by qPCR (ChIP-qPCR) analysis. To further demonstrate that reduction of RORA1 expression could lead to aberrant transcription of novel RORA1 targets, we also conducted shRNA-mediated knockdown of RORA1 and performed RT-qPCR analysis to determine expression of selected RORA1 targets in RORA1-deficient neuronal cells. Biological networks and functions associated with RORA1 transcriptional targets were predicted using Ingenuity Pathway Analysis (IPA) and Pathway Studio 7 programs.

RESULTS

The ChIP-on-chip analysis revealed that as many as 1,338 probes corresponding to promoter regions of 1,274 genes across the human genome were significantly enriched in RORA1-IP DNA (p-value < 0.05; log2 ratio > 0.3). Among these potential targets were genes known to have biological functions negatively impacted in ASD, including neuronal adhesion and survival, synaptogenesis, as well as development of cortex and cerebellum. ChIP-qPCR analysis confirmed binding of RORA1 to promoter regions of selected potential targets, including A2BP1, CYP19A1, HSD17B10, ITTPR1, NLGN1, and NTRK2. Knockdown of RORA1 in the human neuronal cells also resulted in reduced expression of these genes.

CONCLUSION

These findings indicate that RORA1 transcriptionally regulates A2BP1, CYP19A1, HSD17B10, ITTPR1, NLGN1, and NTRK2, all of which have biological functions associated with ASD.
Inducing Mitotic Dyssynchrony in Normal Airway Epithelium Leads to Production of TGF-β1

**BACKGROUND**

Immune-mediated inflammation is currently considered the cause of remodeling in asthmatic airways. However, anti-inflammatory treatments with inhaled corticosteroids do not alter the airway remodeling. Previously, we showed that asthmatic airway epithelium is mitotically dyssynchronous and this dyssynchrony induces basolateral secretion of TGF-β1, an important mediator in fibroblast recruitment and smooth muscle proliferation in asthmatic airway remodeling and a key component in the airway epithelium stress response pathway. Because we consider mitotic synchrony to be a fundamental biological process, we hypothesize that disruption of normal mitotic synchrony will also lead to inappropriate secretion of TGF-β1.

**METHODS**

Normal primary bronchial epithelium from a single donor was grown in parallel in T-75 tissue culture flasks. Starting at -24 hours, the flasks were serum starved for 12 hours in a staggered fashion. At 0 hours, cells from one flask were labeled with membrane dye, PKH-67. The cells were then mixed and grown in complete medium and continuously exposed to bromodeoxyuridine (BrdU). An aliquot of PKH-67 and unlabeled cells were reserved and separately plated as synchronous control populations. Cells and media were collected at 0, 18, 24, 30, 42 and 48 hours. Mitotic phase was analyzed by flow cytometry for 7-AAD DNA staining in BrdU+ cells. Supernatants were analyzed by ELISA for TGF-β1.

**RESULTS**

The mixed culture was mitotically dysynchronous at 0 and 18 hours. The labeled and unlabeled cells began to spontaneously resynchronize at 24 hours and were fully resynchronized by 48 hours. The 24 and 48 hour control flasks remained synchronous throughout the experiment. Baseline TGF-β was measured at 0 hours. Percentage of baseline was calculated for 18 (-9.4%), 24 (-10.3%), 42 (+2.7%) and 48 (+1.8%) hours in the mixed population. In contrast in the control flasks, TGF-β1 percentage of baseline remained low at 24 hours (-10.50%, -8.60%) and 48 hours (-1.81%, -6.45%).

**CONCLUSIONS**

Our data show successful induction of mitotic dyssynchrony in normal cells in which dyssynchrony induces inappropriate secretion of TGF-β1. These data support our previous finding that inappropriate TGF-β1 secretion is the downstream effect of mitotic dyssynchrony. In addition, normal cells spontaneously and rapidly resynchronize. Because asthmatic cells do not spontaneously resynchronize, this suggests the existence of an important intercellular regulatory signal in normal airway epithelial mitosis that is impaired in asthma.
**INSTITUTE FOR BIOMEDICAL SCIENCES**

**DUX4, the FSHD causative gene, regulates pathways in myogenesis and gametogenesis in human RD cells**

**BACKGROUND**

Facioscapulohumeral muscular dystrophy (FSHD) is linked to the deletion of the D4Z4 arrays at chromosome 4q35 subtelomeric region. Each D4Z4 array contains an open reading frame of double homeobox 4 (DUX4), which is aberrantly expressed in patients with FSHD. The aim of this study was to determine transcriptomic response to the ectopically expressed DUX4 protein. Since there is no DUX4 orthologue in mice, our study also evaluated the feasibility of studying DUX4 functions using mouse models.

**METHODS**

We expression profiled human Rhabdomyosarcoma (RD) cells and mouse C2C12 cells (n=4) transfected with expression vectors containing DUX4 for 16 hours using the Affymetrix Human Genome U133 Plus 2.0 Arrays and Mouse Genome 430 2.0 Arrays respectively. Expression vectors containing insertless vectors were used as controls. The data were analyzed using Affymetrix MAS 5.0 followed by Welch t test corrected for false discovery rate (Benjamini Hochberg, 5%) using Genespring GX 11.0. Ingenuity Pathway Analysis (IPA) was used to determine the top canonical pathways regulated by DUX4.

**RESULTS**

Amongst the 2267 transcripts differentially expressed in RD cells, MYOD1 (2-fold), and seven MYOD1 downstream targets (1.3-2.1-fold) were upregulated in RD but not C2C12 cells expressing DUX4 (p<0.05). Furthermore, six transcripts involved in gametogenesis were dramatically induced (171-2805 fold) only in RD cells expressing DUX4. Different canonical pathways were identified by IPA in RD (inflammation, BMP signaling and NRF-2 mediated oxidative stress) and C2C12 cells (p53 signaling, cell cycle and nicotinate/nicotinamide signaling) ectopically expressing DUX4. Among the shared changes of 40 transcripts, UTS2, a potent vasoconstrictor, was dramatically induced by 76-fold and 224-fold in RD and C2C12 cells respectively. The differential expression of MYOD1 and UTS2 were validated by quantitative RT-PCR (p<0.05).

**CONCLUSIONS**

DUX4 regulates different pathways in human RD as well as mouse C2C12 cells as evident by the selective regulation of transcripts involved in myogenesis and gametogenesis only in RD cells as well as identification of diverse pathways in the two cell lines through IPA. These findings suggest that a mouse model expressing human DUX4 will not be a suitable model for studying FSHD.
Towards Proteomic Analysis of an In Vitro Cystic Fibrosis Glandular Acinar Cell Model System

**BACKGROUND**

Mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) affect the functioning of multiple organs in patients with cystic fibrosis (CF), but it is the progression of disease in the lungs that is fatal. In the respiratory tract, CFTR is most highly expressed in the submucosal glands (SMG) where it localizes to the apical surface of ductal and serous cells. In addition, CF glandular acinar cells specifically account for the aberrant physiological functioning of ion fluid in CF glands. Since CF mucus has decreased microbicidal activity and glandular cells are the predominant source of innate immune mediators, we hypothesized that expression and secretion of innate immune mediators is altered in CF glandular acinar cells of the respiratory tract.

**METHODS**

To test the hypothesis, an in vitro three-dimensional acinar model that we had developed with primary human bronchial epithelial cells (Wu X. et al. 2010) was extended to three sets of life-extended CF (ΔF508/ΔF508) and non-CF human bronchial epithelial cell lines (Fulcher M. et al. 2009). The cells were differentiated into glandular acini on a basement membrane matrix. The average diameter of CF and non-CF acini was compared by Image J analysis of brightfield microscopy images. A student’s T-test was performed to test statistical significance. Different glandular mucous and serous markers were detected by fluorescent immunostaining and confocal microscopy.

**RESULTS**

No significant difference was detected between the average diameters of acini formed by three CF and three non-CF cell lines on day 13. Fluorescent immunostaining demonstrated basal polarization (integrin-β6) and formation of a mature lumen by day 15 in CF and non-CF acini. Expression of MUC5B mucin (mucous cell marker) and lysozyme (serous cell marker) on day 17 was also demonstrated in non-CF acini, while the ciliated cell marker β-tubulin IV was not detectable on day 17.

**CONCLUSIONS**

Three CF and three non-CF cell lines differentiated on Matrigel into polarized acini with mature lumens and similar diameters, indicating no difference in acinar size at baseline between cohorts in our model. The expression of mucous and serous cell markers but not cilia cell markers by non-CF acini demonstrate a glandular phenotype. The same markers are being used to characterize CF acini. Next, proteins in basal and apical secretions will be compared between CF and non-CF cohorts using proteomic technologies. Differentially identified proteins will be further analyzed using bioinformatics techniques to better interrogate the pathophysiology of CF lung disease.

(Supported by Children’s National Board of Visitors grants to XW and to MCR)
Brain injury in premature infants remains a major health issue, as improvements in neonatal care that have enhanced the survival of premature infants have also increased the number of premature infants that suffer long-term neurological morbidity. The cellular and molecular mechanisms that govern the response of the perinatal brain to injury remain largely unexplored. One attractive target to prevent or reverse brain injury is the subventricular zone (SVZ), which represents the largest neurogenic niche in the postnatal brain. We have previously demonstrated that, after focal demyelination of the adult white matter (WM), a small population of GAD65 expressing neuroblasts of the SVZ migrate to the area of injury and are redirected from a neuronal to a glial fate by the BMP antagonist Chordin. In this study - using the GAD65-Cre mouse - we examine the response of GAD65-expressing progenitors in the perinatal brain, in particular in a well-established model of brain injury observed in premature infants, chronic perinatal hypoxia (HX; P3-P11). HX results in global and diffuse WM injury. We demonstrate that, after hypoxic injury, there is an increase in the number of cells generated from GAD65-expressing progenitors in the WM, as well as an increase in the percentage of cells generated from GAD65-expressing progenitors in the WM that express the oligodendrocyte lineage markers NG2 and Olig2. Our findings suggest that fate plasticity of neuroblasts also occurs in the immature brain under pathological conditions. Therefore, targeting GAD65-expressing progenitors of the SVZ is a possible therapeutic strategy to repair WM damage observed after hypoxic injury.
Ultrasound-enhanced Delivery of Antibiotics and Anti-inflammatory Drugs into the Eye

**BACKGROUND**

Delivery of sufficient amounts of therapeutic drugs into the eye is often a challenging task. Topical administration of drugs to the cornea is a preferred route for delivery of ocular drugs. However, in most cases less than 5% of the applied drug can actually penetrate through the cornea, and achieving 2-3 times increase in the amount of delivered drugs is considered clinically significant. In this study, ultrasound application at frequencies of 400 KHz-1 MHz, intensities of 0.3-1.0 W/cm², and exposure duration of 5 min was investigated to overcome the barrier properties of cornea.

**METHODS**

Permeability of ophthalmic drugs, Tobraycin and Dexamethasone, and Sodium Fluorescein, a drug mimicking compound, was studied in ultrasound- and sham-treated rabbit corneas in vitro using a standard diffusion cell set-up. Rabbit cornea was placed in a diffusion cell at a normal physiological temperature of 34 °C (in a circulation water bath). Drug solution was added to donor compartment, and receiver compartment was filled with saline. The cornea was exposed to ultrasound for 5 min. After 60 min, solution samples were taken from the receiver compartment to determine concentration of the drug that permeated through the ultrasound- and sham-treated corneas. Light microscopy observations of histology slides were used to determine ultrasound-induced structural changes in the cornea.

**RESULTS**

For Tobraycin, increase in permeability for ultrasound- and sham-treated corneas was not statistically significant. Increase of 46-126% and 32-109% in corneal permeability was observed for Sodium Fluorescein and Dexamethasone, respectively, with statistical significance (p<0.05) achieved at all treatment parameters as compared to sham-treated corneas. This permeability increase was highest at 400 kHz, and appeared to be higher at higher intensities applied. Histological analysis showed structural changes which were limited to epithelial layers of cornea.

**CONCLUSIONS**

Ultrasound application provided enhancement of drug delivery, increasing the permeability of the cornea for the anti-inflammatory drug Dexamethasone. Future investigations are needed to determine effectiveness and safety of this application in vivo in long-term survival studies.
Nonlinear Vocal Fold Dynamics in a Two-Mass Model of Speech Arising from Asymmetric Intraglottal Flow

BACKGROUND
Voiced speech is initiated when a critical lung pressure forces the vocal folds apart, inciting self-sustained oscillations. The aerodynamic forces interact with the tissue properties to produce the vocal fold dynamics. During the closing phases of speech, asymmetric flow formations prevail, with flow attachment to one vocal fold wall. In the case of unilateral vocal fold paralysis, one vocal fold loses muscular control, creating a tension imbalance between the opposing folds. The objective of this work is to investigate how asymmetric flow fields which occur during the closing phases of the phonatory cycle, and which drive vocal fold motion, interact with irregularly tensioned vocal folds in the case of unilateral vocal fold paralysis.

METHODS
A reduced order vocal fold model, consisting of a coupled spring-mass-damper system is coupled with a refined theoretical fluid solver that provides a boundary-layer estimation of the asymmetric pressures (BLEAP) for asymmetric flow through the vocal folds. This flow model is an advancement over existing 1-D, symmetric, inviscid Bernoulli flow solvers that are overly simplistic. The dynamics of the model vocal folds arising from the fluid-structure interactions with the BLEAP flow model are analyzed using nonlinear analysis via phase-space reconstruction with a Volterra-Weiner-Korenberg series in order to elucidate the emergence of nonlinear dynamics.

RESULTS
Asynchronous vocal fold motion is plotted as a function of the subglottal driving pressure and tension asymmetry. Results are also contrasted between the more physically-realistic BLEAP flow solver, and the Bernoulli flow solver. The domain of irregular motion is found to be much greater using the refined asymmetric flow solver. The coupling of asymmetric flow and vocal fold tension is found to produce chaotic vocal fold motion, although only for symmetry parameters less than 0.8. The findings are well correlated with clinical observations of vocal fold dynamics in patients with unilateral paralysis.

CONCLUSIONS
While there is a negligible impact on vocal fold dynamics for very slight tension irregularities (> 0.8), a critical value exists where the interplay between the asymmetric tension, and asymmetric fluid loading incites chaotic vocal fold oscillations. While current surgical remediations for vocal fold paralysis focus on restoring proper geometry, these results indicate that restoring symmetric tension is also crucial to restoring normal voice quality.
Potential disease specific role for a de-ubiquitinating enzyme, ubiquitin carboxyl-terminal hydrolase isozyme L1 (UCHL1) in myositis

BACKGROUND

Idiopathic inflammatory muscle diseases (myositis) such as polymyositis, dermatomyositis, and inclusion body myositis are characterized by severe muscle weakness, elevated levels of serum muscle enzymes and muscle inflammation. Others and we have shown that endoplasmic reticulum (ER) stress, autophagy and hypoxia have pathogenic role in myositis. However, the interaction between these processes and their specific relationship to myofiber damage in myositis has not been completely elucidated. We hypothesize that the chronic ER stress triggered in myositis muscle due to unusual overexpression of major histocompatibility class I (MHC) activates ubiquitin proteosome pathway (UPP) and further cause proteolytic degradation and muscle loss in myositis. Here we utilized conditional transgenic mouse model that over expresses MHC class I in skeletal muscle to test the hypothesis.

OBJECTIVE

To understand the role of UPP in myopathic muscle using mass spectrometry based novel in vivo stable isotope (13C)-'labeled' mouse proteomic strategy.

METHODS

Muscle lysate from 'unlabeled' conditional MHC class-1 transgenic mice and the age matched 'labeled' C57BL6 mice were obtained. Lysates were mixed (1:1), electrophoresed and individual bands were tryptic digested and global protein alterations were identified using LC-MS/MS. Disease specific proteomic modulations were identified and validated using specific antibody based biochemical assays [n=4 mice/group]. Tissue interstitial fluid was obtained by microdialysis of muscle and analyzed for the presence of UPP members.

Contd on next page
RESULTS

A total of 829 proteins were accurately quantified in the muscle of which ~53% proteins were differentially modulated between control vs diseased muscle. We used dystrophin deficient skeletal muscle as a myopathic control. Out of differentially modulated proteins 24 belong to UPP and these proteins show >2 fold up-regulation compared to controls. We have identified ubiquitin carboxyl-terminal hydrolase isozyme L1 (UCHL1), a de-ubiquitinating enzyme to be specific to myositis muscle. Further analysis of differentially modulated proteins supported the activation of other members of ER stress response and UPP in myositis muscle. The specificity and the increased expression of UCHL1 was validated using independent set of samples. Interstitial fluid from myopathic muscle demonstrated disease specific increase of UCHL1 suggesting its role as a potential biomarker for myositis. The specific involvement of UCHL1 and other members of UPP in muscle damage in myositis are currently being investigated.

CONCLUSION

Enhanced expression of UCHL-1 and the activation of UPP might be the connecting link between chronic ER stress and muscle fiber degeneration in myositis. UCHL-1 might be a potential biomarker for disease progression in myositis.
Morpholino treatment improved muscle function in Pitx1 transgenic mice

**BACKGROUND**
Paired-like homeodomain transcription factor 1 (PITX1) was proposed to be critically involved in facioscapulohumeral muscular dystrophy (FSHD). We generated a tet-repressible muscle-specific Pitx1 transgenic mouse model in which expression of Pitx1 can be induced in skeletal muscle. In this study, we attempted to knock-down Pitx1 expression using morpholino molecules designed to block translation of the Pitx1 mRNA.

**METHODS**
Three groups of Pitx1 transgenic mice (n=5) received weekly IV injections of phosphorodiamidate morpholino oligomers (PMO) (100mg/kg), arginine-rich cell-penetrating peptide conjugated PMO (PPMO) (10mg/kg), or saline for six weeks. A group of single transgenic control littermates were used to provide baseline expression level of Pitx1. The mice received the first injection of morpholinos when the oral doxycycline was discontinued to induce Pitx1 expression. Four weeks after Pitx1 induction, muscle function of the mice was evaluated by grip strength and rotarod tests. Triceps and quadriceps muscles were collected for H&E, Immunohistochemistry and immunoblotting at the end of the 6th week.

**RESULTS**
Grip strength data showed that treatment with PPMO significantly (p<0.05) improved muscle function of the transgenic mice over-expressing Pitx1 while the PMO treatment did not improve the muscle function. Immunohistochemistry and immunoblotting data showed that PITX1 protein expression in the muscle was reduced by the PPMO treatment but not PMO treatment. The pathology of the muscles of mice treated with PPMO was improved by showing less angular atrophic fibers and central nuclei.

**CONCLUSIONS**
Pitx1 mice showed significant improvement in both muscle function and pathology after receiving PPMO injections. The results suggest that morpholinos can be an option for treatment development for FSHD.
VPS53 polymorphism destroys miR-206 binding and is associated with bone and muscle phenotypes in young males and females

OBJECTIVES

MicroRNA-206 is an mRNA translational regulator found exclusively in skeletal muscle, which has been associated with proper myocyte differentiation. The purpose of our study was to determine if a genetic variant within the VPS53 gene miRNA-206 binding site (rs7219151) is responsible for phenotypic differences in muscle and bone strength and size.

METHODS

We genotyped the single nucleotide polymorphism (SNP), rs7219151, in the miRNA-206 binding site (intron) of the VPS53 gene in a cohort of 779 healthy, white males and females (average age 24) from the FAMuSS study. Measurements of upper arm muscle volume, strength (1-repetition max [1RM] and force transducer), and cortical bone volume were collected before and after resistance training. Hardy-Weinberg equilibrium was tested using a chi-square test. Associations between mean phenotypes and genotypes were tested using an ANCOVA with age and baseline weight as covariates (cortical bone adjusted for age only). For those associations showing a significant F-test, pair-wise post hoc comparisons were performed and resulting p-values adjusted for multiple comparisons using the Sidak method.

RESULTS

Females homozygous for the G allele (G/G, n=90) for the rs7219151 SNP demonstrated significantly lower baseline total bone cross-sectional area compared to heterozygous females (G/A, n=164, p=0.04) and females homozygous for the A allele (A/A, n=55, p=0.03). Additionally, males who were homozygous for the G allele had a significantly lower baseline 1-RM strength than males homozygous for the A allele (p=0.03).

CONCLUSIONS

Small bone size is known to be associated with increased fracture risk. We found that the rs7219151 SNP is associated with a sex-specific decrease in bone cross-sectional area in females, thus further study of this variant may help elucidate a marker for increased fracture risk. We also determined that rs7219151 is associated with a decreased baseline 1-RM strength in males, which supports previous data indicating that miRNA-206 is important for proper skeletal myocyte differentiation.
BP1 Protein, a Transcription Factor Associated with Clinically Aggressive Breast Cancer, is Secreted in Exosomes

BACKGROUND
BP1 is a member of the homeobox gene family, which encode transcription factors. Our laboratory discovered that BP1 is associated with breast cancer progression and clinically aggressive breast cancer. We have observed that BP1 is secreted from breast cancer cell lines, but not from normal breast epithelial cell lines, and have established that the primary mode of secretion is in exosomes. Exosomes are small vesicles (30-100 nm) that originate in the Golgi, are secreted from a variety of cell types, and have been isolated from biological fluids, such as serum and urine.

METHODS
MCF-7, MDA-MB-231, and T47D cells were grown for 48 hours in serum free (SF) media. BP1 protein was detected in the conditioned media (CM) of cell lines by concentrating the media about 300 fold. The media was subsequently taken through a series of centrifugations to separate exosomes from other vesicles and debris. Viability of MCF-7 cells was assessed using an MTT assay. Transmission Electron Microscopy was used to obtain images of exosomes from MCF-7 and HS-578T cell lines.

RESULTS
We have successfully demonstrated the presence of BP1 protein (pBP1) in exosomes secreted by MCF-7, MDA-MB-231, and T47D breast cancer cells. This data is corroborated by EM images of exosomes secreted by MCF-7 and HS-578T cells. MCF-7 cells, grown in the presence of exosomes isolated from MCF-7 cells engineered to overexpress BP1, increased MCF-7 cell proliferation 6 fold by day 3 of incubation, while MCF-7 cells incubated with exosomes from MCF-7 control cells containing an empty vector showed increased proliferation of only 2.5 fold by day 3. Western blot analysis showed that pBP1 was present in serum from women with metastatic breast cancer in 5 out of 8 cases but was absent in all 5 serum samples tested from normal women.

CONCLUSION
Our data suggest that secreted pBP1 may play a role in influencing the tumor microenvironment by stimulating tumor cell proliferation. The fact that there appears to be more secreted pBP1 in serum of women with metastatic breast cancer suggests that pBP1 might be useful in early detection, predicting prognosis and/or monitoring therapy.
Proteomic analyses of sinonasal secretions of pediatric patients with or with chronic rhinosinusitis

BACKGROUND/OBJECTIVES

Chronic rhinosinusitis (CRS) is a highly prevalent upper respiratory disease characterized by mucous overproduction and hyperplasia of submucosal glands in the sinus mucosa, which primarily express MUC5B mucin. The mucin and protein composition of sinonasal secretions, however, is minimally characterized. The objectives of this study were to perform proteomic analyses to identify the protein composition of sinonasal secretions, including the specific mucins, and to determine whether MUC5B mucin is markedly increased in sinonasal secretions from pediatric patients with CRS.

METHODS

Sinus secretions were collected from (a) CRS patients undergoing functional endoscopic sinus surgery and (b) control patients without CRS undergoing surgical procedures at CNMC. Secretions were processed for proteomic analysis using well-established protocols in the Proteomics core at CNMC. Proteins were separated by SDS-PAGE gel electrophoresis; bands were excised, trypsin-digested, and analyzed using liquid chromatography tandem mass spectrometry (LC-MS/MS) on a linear trap quadrupole (LTQ) mass spectrometer. Proteins were identified using the Sequest algorithm in the Bioworks Browser Software against the UniProt database. Western blot analyses were performed to validate the results.

RESULTS

Four samples from CRS patients and 1 from a non-CRS patient have been analyzed by proteomics to date. Proteomic analyses identified MUC5B mucin in all CRS samples but not in the control sample. MUC5AC mucin was identified in two CRS samples with a unique peptide count in each that was less than that of MUC5B. Glutathione S-transferase and parkinson protein 7, which have been previously reported to be highly expressed in CRS tissues, were identified in all 4 CRS secretion samples. Additionally, alpha-1-antitrypsin, glycoprotein-340, PLUNC and calgranulin-B were identified in sinonasal secretions and are being validated by Western blot analyses. Finally, Western blot analyses validated the presence of MUC5B in CRS but not in the non-diseased sample and minimal to no expression of MUC5AC mucin in any sample.

CONCLUSIONS

Preliminary results indicate that MUC5B is the primary mucin present in sinonasal secretions from CRS patients, while control secretions appear to have minimal mucins present. Many of the other identified proteins are involved in innate immunity, metabolic processes, and response to stress. Further investigation by proteomic analysis and validation by western blot analysis of proteins present in CRS secretions may provide more insight into the pathogenesis of CRS in pediatric patients. Currently, more specimens are being analyzed to expand and further validate the proteomic results using a larger number of samples from CRS and control patients.
Asynchronous cycles of muscle degeneration leads to cell death pathways in adjacent normal muscle

BACKGROUND
Duchenne muscular dystrophy (DMD) shows age-related failure in muscle regeneration. In normal individuals, injured skeletal muscle shows successful regeneration. We hypothesized that successful regeneration is done synchronously over 2 weeks, whereas DMD muscle shows recurrent bouts of degeneration leading to asynchronous and ultimately unsuccessful regeneration. Further, we hypothesized that asynchronous remodeling would induce inappropriate signaling and fibrogenic networks, both in neighboring asynchronous regions, as well as adjacent normal muscle. We sought to test this model using cycles of induced degen/regen in normal muscle, with localized analysis of cross-talk between regions in different stages of the 2 week regeneration window.

METHOD
Notexin was used to induce muscle degeneration through local intramuscular injection. Each muscle had two injections done either 4 days or 10 days between injections, each labeled with a dye. Mice were sacrificed 13-17 days after the final injection, muscle flash frozen in isopentane cooled in liquid nitrogen, and cryosections cut. LCM was used to collect neighboring red and blue regions (asynchronous regeneration), as well as the normal muscle in between the two areas. mRNA profiling was done on triplicate areas (serial sections) of each region (4 days vs. 10 days; 4 regions (red, blue, between, normal); triplicates; n= 24 Illumina microarrays).

RESULTS
Normal muscle between 4 day asynchronous regenerating regions showed evidence of histone modulation, mitochondrial disruption and inflammatory response (CD74). In contrast, muscle between 10 day regions was considerably less pathological, consistent with our hypothesis. The regenerating regions at 4 day intervals showed inappropriate induction of fibrogenic pathways.

CONCLUSION
To our knowledge, we provide the first experimental evidence that regenerating regions of muscle have a deleterious effect on neighboring regions if they are in different stages of the 2 weeks regeneration time frame. This provides a model for failed regeneration and weakness in DMD.
Preliminary Endoscopic Results of Acute and Late Rectal Toxicities in Patients Treated with Radiosurgery for Prostate Cancer

BACKGROUND
Radiation therapy is a well-established treatment modality for clinically localized prostate cancer. Radiotherapy delivered with the CyberKnife radiosurgical device could potentially minimize rectal toxicity by reducing the volume of rectum irradiated to high doses and through exploiting the potential radiobiologic benefits of hypofractionation. The goal of this study is to determine the clinical and endoscopic toxicity of radiosurgery when used as monotherapy and as a boost in addition to IMRT.

METHODS
All patients who were treated at Georgetown University Hospital with CyberKnife radiosurgery for clinically localized prostate cancer and who received a post treatment colonoscopy were identified. Patients were treated with either 5 fractions of radiosurgery as monotherapy or 3 fractions of CyberKnife radiosurgery as a boost. Patients’ rectal toxicity was graded using the Common Terminology Criteria for Adverse Events Version 4 (CTCAE v.4) and the Vienna Rectoscopy Score (VRS). Descriptive statistics were used to characterize our patient population. Fisher’s exact test was utilized to compare the treatment outcomes between patients treated with CyberKnife as monotherapy vs. boost.

RESULTS
36 patients were included in the study. 17 were African American and 19 were Caucasian. Median age at treatment was 66 (range 58-83). Median follow up was 24 months (range 18-47). Median time of the last post-treatment colonoscopy was 12 months (range 1-30). 23 patients were treated as monotherapy (median dose 36.25 Gy), and 13 as a boost (median dose 19.5 Gy with median dose of 45 Gy as external beam radiotherapy). Thirteen patients received hormonal therapy during the course of their radiotherapy. 9, 20, and 7 patients were identified as low risk, intermediate, and high risk respectively. 14 (38%) and 19 (52%) patients had a grade 1-2 acute (≤ 6mo) and late (> 6mo) rectal toxicity, respectively per CTCAE v.4. No patients had a grade 3 or higher rectal toxicity. 6 patients were observed to have telangiectasias and 2 patients had mucosal edema on colonoscopy per VRS. No patients were observed to have a score of 3 or higher on VRS. No patients had rectal ulcerations, strictures, or necrosis. 3 patients (23%) in the boost group and 3 patients (13%) in the monotherapy had telangiectasias on colonoscopy (p=0.65). Both patients with congested mucosa were in the boost group (p=0.12).

CONCLUSIONS
CyberKnife radiosurgery as boost or monotherapy for the treatment of localized prostate cancer has acceptable early and late rectal toxicity in this preliminary study that is comparable to external beam radiotherapy. Future prospective studies will be needed to confirm our observations.
SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Socioeconomic Factors Affecting CML in India

BACKGROUND

Data from 13,790 Indian patients with CML have been collected by The Glivec® International Patient Assistance Program (GIPAP) which supplies doses of Imatinib free of cost in developing countries. The available information from this project has allowed us to look at environmental factors and age at onset in regard to possible etiologic agents and response to treatment.

METHODS

Pts were enrolled in GIPAP starting in 2002 after a diagnosis of CML (Philadelphia Chromosome + or BCR-ABL1 +) and completion of a financial evaluation confirming the inability to pay for treatment with Imatinib. Overall survival (OS) for pts enrolled between 2003 and 2007 was estimated using the Kaplan-Meier method considering the time from approval in the program until death or censored at the date of last contact. Cox Proportional Hazards models were created stratified by age group.

RESULTS

Of the 13,790 Indian pts with CML entered into GIPAP, 586 were <15 yo and 996 were > 60. The median age of 32 was significantly less than the U.S. median age (66). Age of onset increased as income level increased. Phase of CML at diagnosis was predominantly in the chronic phase (84.4%) followed by blast crisis (5.7%) and accelerated phase (5.5%). OS was poorest in pts >65 and best in pts 15-64. Delay in treatment had a significant effect on survival and decreased 2002-2007.

CONCLUSIONS

Environmental factors such as socioeconomic status appear to contribute to early age of onset and differences in 1-year OS exist by age. Advanced phase of disease at diagnosis and longer time from diagnosis to initial dose were associated with poorer outcomes.
BACKGROUND

Pediatric Chronic Myeloid Leukemia (CML) is a relatively rare disease representing approximately 3% of all childhood leukemia. The age-specific incidence of pediatric CML for ages 0-19 is approximately 0.03% per 100,000 (SEER 9 Registries 1973-2008). The purpose of this study is to describe the demographic characteristics and survival of pediatric CML patients in GIPAP and assess independent risk factors for death including country of diagnosis, gender, age and phase at diagnosis.

METHODS

More than 33,000 patients from Europe, Latin America, Asia and Africa were enrolled (2002-2010) of which 3,188 were between 0 and 20 years. Data was collected by the Max Foundation. Means and proportions were estimated along with Kaplan-Meier estimates of overall survival (OS). Cox proportional hazards models were created to assess prognostic factors associated with the risk of death.

RESULTS

A majority (78%) of the patients were from Asia including India (n=1140), China (n=384), Pakistan (n=261) and South-eastern Asia (436). Distribution of sex varied by region; Asia-65%, Europe-60%, Latin America-54% and Africa-51% were male (p<0.0001). The majority (77.0%) of patients were diagnosed in the chronic phase with variation by region. 36% of patients from Europe were diagnosed in the Accelerated phase as compared to 8% from the other regions (p<0.0001). Africa had the highest proportion of patients <10 years (15%) while patients from Europe had the highest proportion of patients between 15-20 years of age (79%). The mean age of diagnosis in the pediatric population was 14.6 and patients from Europe were significantly older as compared to patients from Africa (p<0.05). There were 177 deaths between 2002 and 2007. 3-year OS probability was 88.9% (95% CI: 87.3-90.4). No statistically significant difference exists by gender, age at diagnosis or region. Patients diagnosed in chronic phase had a 3-year OS of 93.9% (95% CI: 92.4-95.2), accelerated 79.1% (95% CI: 71.1-85.2) and blast crisis 35.3% (95% CI: 25.6-45.2).

CONCLUSIONS

Differences exist within the GIPAP cohort including the proportion of patients who were male, age at diagnosis and phase of disease at diagnosis. However, only phase of disease at diagnosis was considered an independent risk factor. Through this analysis, we show that pediatric CML accounts for approximately 10% of CML patients from developing countries with about a 10% mortality rate that increases with more advanced phase of disease. Further research is warranted to understand the impact of an earlier age at diagnosis among developing countries.
A Descriptive Epidemiological Study of Lobular Carcinoma, an Uncommon Form of Breast Cancer

BACKGROUND

Lobular carcinoma (LC) is a distinctive neoplasm originating in the milk producing glands, constituting 10-12% of all cases. We conducted a descriptive epidemiological study of LC, the second most common type of breast cancer in the U.S., and compared it with the pathogenesis of infiltrating ductal carcinoma.

METHODS

A total of 86,846 cases of invasive LC (ILC) from women, aged 20 to 85, were obtained from NCI’s SEER Program for the years 1973-2008 in the United States. There were 20,512 cases of LC in-situ (LCIS) and 66,634 cases of ILC. For comparison, 692,201 cases of IDC and 61,569 cases of ductal carcinoma in situ (DCIS) were collected. The analysis compared trends, age specific rates, log-log plots, age frequencies and relative survival rates.

RESULTS

From 1973-2008, the age-adjusted rate of LC progressively increased from 5.8 to 16.4/ 100,000 women. In an age frequency analysis of age versus rate, LCIS increased to 0.22/ 100,000 women at age 50, and then declined to 0.02/100,000 women at age 80. ILC increased to 0.11/100,000 women at age 50, and then plateaued after menopause but did not decline. Log-log plots revealed parallel curves between ILC and IDC in both pre-menopausal and post-menopausal age groups. At age 50, the age specific rate of LCIS increased to 11.3/100,000 women then progressively decreased. In contrast, the age specific rate of DCIS was 22.1/100,000 women at age 50 and continued to increase after menopause.

CONCLUSION

At menopause, the incidence of LCIS decreases as a result of lobular involution of the breast. In contrast, DCIS continues to increase. ILC does not decline but plateaus suggesting that the initiation of LC occurs before menopause, but the tumor becomes clinically apparent only after menopause. Although morphologically different, parallel log-log plots and age frequency analysis suggest a similar pathogenesis for IDC and ILC even though epidemiological patterns are different.
Secondary Inflammatory Breast Cancer: A Possible Model for Post-Surgical Dissemination of Cancer

BACKGROUND

The phenomenon of accelerated tumor growth following surgery has been observed repeatedly and merits further study. Inflammatory breast cancer (IBC) is widely recognized as an extremely aggressive malignancy characterized by micrometastases at the time of diagnosis, with one interesting subgroup defined as secondary IBC where pathologically identifiable IBC appears after surgical treatment of a primary non-inflammatory breast cancer. One possible mechanism can be related to the stimulation of dormant tumor cells through local angiogenesis occurring as part of posttraumatic healing. It is therefore possible that secondary IBC can be used as a model to support local angiogenesis as an important contributor to the development of an aggressive cancer.

METHODS

Cases of secondary IBC were identified in a review of patients referred to the IBC Registry (IBCR). The IBC Registry was developed to provide a standardized population of IBC patients for epidemiologic and laboratory studies, and among the 156 patients enrolled thus far, eight were identified as having secondary IBC. In this report we document the histories of three patients with secondary IBC as well as two additional patients whose disease presentation also supports the possible occurrence of IBC secondary to breast trauma.

RESULTS

Two of the patients with Secondary IBC developed pathologically confirmed dermal lymphatic invasion two and 42 months after partial mastectomy for non-inflammatory breast cancer. The third patient had been apparently free of recurrence for seven years when she had reconstructive surgery, which was followed by IBC seven months later. Two additional cases are presented, one in which IBC manifested one month following ductogram procedure. The other patient was diagnosed with IBC one year following nipple piercing and ring removal.

CONCLUSIONS

Recent publications have focused on the role of surgery in the subsequent development of metastatic breast cancer, many of them focusing on a hormonal mechanism triggered by removal of the primary tumor. We propose local angiogenesis as another possible mechanism for post-surgical dissemination of cancer. In view of the hypothesis that trauma can stimulate angiogenesis which can accelerate tumor growth, the documentation of IBC appearing at the site of a traumatic event merits consideration. Our experience with IBC, noted in the case reports above suggest that local trauma probably mediated in large part by angiogenesis can be an important trigger of IBC. We would therefore suggest that Secondary IBC be considered for investigation of one possible mechanism for post-surgical tumor dissemination.
Patient Navigation Significantly Reduces Delays in Breast Cancer Diagnosis in the District of Columbia

BACKGROUND
Patient Navigation (PN) originated in Harlem, NY as an intervention to help poor women overcome access barriers to timely breast cancer treatment. Despite rapid, nationally widespread adoption of PN, empirical evidence on its effectiveness is lacking. This led NCI’s Center to Reduce Cancer Health Disparities to initiate a multi-center research effort in 2005 to measure the effectiveness of PN for several cancers. The GW Cancer Institute, as a project participant, established the D.C. Citywide Patient Navigation Research Program (DC-PNRP), with one objective being determination of PN effectiveness in reducing diagnostic delays (number of days from abnormal screening to definitive diagnosis).

METHODS
Our sample included 2,678 women (1,049 navigated; 1,629 concurrent records-based controls) examined for breast cancer from 2006-2010 at nine hospitals/clinics in DC. Analyses included only women who reached complete diagnostic resolution. Significant differences in diagnostic time between navigated and control women were tested with ANOVA models adjusted for race/ethnicity, health insurance, age at abnormal screening, and biopsy as the definitive test. Log transformations normalized diagnostic time. Geometric means were estimated and compared using Tukey-Kramer p-value adjustments.

RESULTS
Adjusted average—geometric mean (95% CI)—diagnostic time (in days) was significantly shorter for navigated women, 25.1 (21.7, 29.0), than controls, 42.1 (35.8, 49.6). Adjusted average diagnostic time was significantly shorter for biopsied navigated women, 26.6 (21.8, 32.5), non-biopsied navigated women, 27.2 (22.8, 32.4), and non-biopsied controls, 34.9 (29.2, 41.7), than biopsied controls, 57.5 (46.3, 71.5).

CONCLUSIONS
Navigated women, especially those requiring biopsy, reached their diagnostic resolution significantly faster than controls.
Compassion Fatigue among Oncology Nurses

INTRODUCTION

The amount of human suffering and loss that occurs in caring for cancer patients, can take an enormous amount of physical, spiritual, emotional and professional toll on cancer care providers. This descriptive, cross-sectional survey was conducted in inpatient nursing units and outpatient clinics in a major cancer center, to examine the common factors influencing Compassion Fatigue (CF) among oncology nurses and to identify resources available to alleviate the problem.

METHODS

A sample of 247 hands-on and clinical research oncology RNs were invited to participate in this survey. The demographic profile and a 30-item Professional Quality of Life revised edition five (ProQOL R-V) scale were used for measuring CF, compassion satisfaction, and burnout among the participants. A series of cross tab analyses examined the relationship between participant demographics and three ProQOL R-V subscales. Narrative questions elicited trigger situations and coping strategies.

RESULTS

The study findings show CF scores were significantly different between nurses who worked at the bedside and clinical research. Approximately 85% of the participants had scores indicating risk for CF. There were significant differences in compassion satisfaction, according to the areas of work and the primary shift of the day nurses work. The most common category of trigger situations was caring for the patient. Work-related and personal coping strategies were also identified.

CONCLUSION

Study findings are consistent with prior research findings that understanding and being able to recognize the symptoms of CF, and knowing how to manage and prevent the negative consequences can be critical to the personal and professional health of the nurse.

KEY WORDS

Compassion satisfaction; Burnout; Compassion Fatigue; Nursing; Caring, Work environment
BP1 Activation of c-Myc and Twist in African American Breast Cancer Cell Lines

INTRODUCTION
BP1 is a transcription factor and a member of the homeobox gene family. BP1 is activated in 89% of the tumors of African American women (AAW) compared with 57% of the tumors of Caucasian American women (CAW). AAW with breast cancer have larger tumors and an almost 50% higher mortality rate than CAW. BP1 expression is also associated with larger and more aggressive tumors, suggesting BP1 may contribute to the aggressiveness of tumors of AAW. We set out to identify molecular pathways underlying the discrepancy of breast cancer aggressiveness in AAW and CAW.

METHODS
Characterization of breast cancer cell lines derived from tumors of AAW and CAW was performed using Western blot analysis. RNA was extracted from these cell lines for microarray experiments to identify molecular pathways underlying the racial disparity in breast cancer. Microarray analysis was performed using Partek and Ingenuity Pathway Analysis. Validation of microarray data was done using qPCR and Western blot analysis.

RESULTS
We have analyzed gene expression in five cell lines derived from tumors of AAW (cAAW) and five cell lines derived from CAW (cCAW). We found that: (1) cell lines from AAW overexpress BP1 more frequently than cell lines from CAW. (2) Our previous data showed that BP1 is involved in the epithelial to mesenchymal transition (EMT). Preliminary analysis revealed that the TWIST gene, a trigger of EMT and a direct target of BP1, is represented more frequently in the cell lines from AAW compared to their CAW derived counterparts. (3) C-MYC, an important oncogene, is also preferentially activated in cell lines from AAW than CAW. Validation experiments confirmed the microarray results in both MCF-7 cell lines and Hs578T cell lines.

CONCLUSIONS
Our data identify several molecular pathways that may be frequently activated in breast cancer of AAW, including EMT and C-MYC. The genes that are overexpressed in tumors of AAW compared with tumors of CAW may make good therapeutic targets. This approach also has the potential of developing more effective therapies for the many AAW whose tumors are both BP1 positive and have activated specific pathways downstream of BP1. Further studies will be needed to determine whether any of these genes, alone or in combination, is prognostic.
Implications of Axillary Lymph Node Dissection on Management of Breast Cancer Patients

OBJECTIVES
Among patients with limited sentinel lymph node metastasis, the American College of Surgeons Oncology Group (ACOSOG) Z0011 Trial demonstrated that axillary lymph node dissection (ALND) had no survival benefit compared to sentinel lymph node biopsy (SLNB) alone. However, ALND provides information about the number of additional lymph nodes containing metastases, which may lead to implications for treatment. The purpose of our study was to determine whether ALND impacted the recommendations for chemotherapy and radiation therapy for breast cancer patients as opposed to SLNB alone.

METHOD
We retrospectively queried our breast care center’s database to identify patients with 1 to 3 positive sentinel lymph nodes who had undergone ALND between October 2001 and June 2011. Unlike ACOSOG Z0011, mastectomy patients were included in this study. Age, race, pertinent family history, oncotype score, pathological diagnosis (including size, stage, receptor status, and lymphovascular invasion), operative reports, SLNB results, and ALND results were collected. A group including experienced medical oncologists and radiation oncologists were presented the information with SLNB results alone and asked to provide treatment recommendations. The group was then presented the ALND results and asked to provide treatment recommendations. The results were then analyzed for changes in recommendations.

RESULTS
Out of the 100 total patients, 53 patients (53.0%) did not have any additional positive lymph nodes on axillary dissection. As a result, there was no change in treatment recommendations for those patients. There were 25 patients (25.0%) with positive axillary lymph node metastasis who did not have modifications to the treatment recommendations. As a result, 78.0% of patients did not have any changes in treatment recommendations following ALND. The treatment recommendations were modified in 23 patients (23.0%) who had additional positive axillary lymph nodes. Of the 23 patients, 13 had mastectomies and were recommended postmastectomy radiation and 4 had changes in recommended chemotherapy based on the ALND results. Of the 10 breast conservation patients, 8 were recommended supraclavicular radiation, 1 had a change in recommended chemotherapy, and 1 had changes in both chemotherapy and radiation recommendations.

CONCLUSION
Treatment recommendations were not modified in the majority of patients based on ALND, and over half of the patients had no additional positive lymph nodes. This study supports that SLNB alone provides sufficient information for appropriate treatment of breast cancer patients undergoing breast conservation.
Monoclonal antibody against Nicastrin as a novel therapeutic for invasive breast cancer

Nicastrin is an essential component of the gamma secretase (GS) enzyme complex, required for its synthesis and recognition of substrates for proteolytic cleavage. The purpose of this study was to investigate whether nicastrin has prognostic value or potential as a therapeutic target in breast cancer. The suitability of nicastrin as a target in breast cancer (BC) was assessed using BC tissue microarrays (TMAs) (n = 1050), and its biological role in vitro was evaluated in BC cell lines following gene silencing. Nicastrin blocking antibodies were developed and their suitability as potential clinical therapeutics evaluated. TMA and cell line analysis confirmed that nicastrin expression was upregulated in BC compared to normal breast cells. In TMA patient samples, high nicastrin expression correlated with ER expression and patient age. In pre-defined subset analysis, high nicastrin expression predicted for worse BC specific survival in the ER -ve cohort. Anti-nicastrin polyclonal and monoclonal Abs were able to decrease the invasive potential of BC cells. This supports our hypothesis that a Nicastrin blocking antibody could be used to limit metastasis in invasive BC.
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Effect of Lab Collection Frequency on Anti-metabolite Dosage and Infectious Outcomes in Pediatric Acute Lymphoblastic Leukemia (ALL) Patients on Maintenance Chemotherapy

BACKGROUND

Current chemotherapy protocols for ALL conclude with a maintenance phase, a multi-year regimen given to patients in remission. The backbone of this phase is a combination of two oral anti-metabolite drugs: 6-Mercaptopurine (6MP) (given daily) and Methotrexate (MTX) (given weekly). It has been demonstrated that the cumulative doses of 6MP/MTX have important prognostic implications and higher dose intensity is correlated with better outcomes. Dosages of 6MP & MTX must be routinely adjusted due to variations in white blood cell (WBC) and absolute neutrophil (ANC) counts to prevent vulnerability to infection due to neutropenia. Routine immunological monitoring often leads to 6MP/MTX dose adjustments and, occasionally, to withholding of chemotherapy altogether to allow for counts to recover. Historically, counts are monitored either once every two weeks or four weeks, owing to a long-standing debate among providers about the benefit of each time interval. More frequent monitoring may be subject to misinterpretation of natural fluctuations in cell counts and may result in withholding medication more often, leading to lower cumulative 6MP/MTX doses and worse prognosis. Conversely, less frequent monitoring may delay detection of neutropenia and predispose patients to infection. This study aims to determine if an optimal time interval for lab collection exists, to minimize the infectious complications and days held from chemotherapy, maximize the cumulative therapeutic 6MP/MTX doses received, and ensure the best possible outcome in ALL patients.

METHODS

A retrospective chart review included 100 pediatric patients with B-cell ALL treated at Children's National Medical Center and The Center for Cancer and Blood Disorders of Northern Virginia between the years 1985 and 2009. Patients were selected at random from a clinical leukemia database and data was collected on an equal number of participants at each center. Data points covered the duration of maintenance therapy using a longitudinal study design.

CURRENT STATUS

Data is being transferred into REDCap (Research Electronic Data Capture), a web-based research support software. Patients will be divided into two cohorts according to average visit frequency to the outpatient oncology clinic (2 or 4 week intervals) and adjusted for maintenance protocol followed. End points for comparing cohorts include cumulative 6MP/MTX dosage (mg/m2/day or week), number of days chemotherapy was withheld, number of clinically or microbiologically diagnosed infections, and number of hospital admissions for febrile neutropenia.

RESULTS

Pending
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Interpretation Time of 3D Automated Breast Ultrasound (ABUS)

RATIONALE AND OBJECTIVES

Because the sensitivity of mammography declines with increasing breast density, handheld ultrasound (HHUS) has been suggested for adjunct screening of women with dense breasts. However, HHUS can require up to 20.8 minutes of physician time per bilateral examination. 3D automated breast ultrasound (ABUS) is a promising new technique for screening women with dense breasts, as the only physician time required is in image interpretation. This approach may allow for efficient integration of adjunct screening ultrasound in clinical practice. The purpose of this study is to quantitatively assess physician time required for ABUS interpretation.

MATERIALS AND METHODS

Three radiologists were timed while interpreting ABUS cases acquired as part of a multi-institutional prospective trial. Timing began when the radiologist accessed the ABUS images and ended when the final report was generated, with a total of 75 studies timed.

RESULTS

To interpret an ABUS examination, Radiologist A required 63.4s-272.6s (mean 150.0s, SD 51.8s); Radiologist B required 114.8s-615.4s (mean 234.0s, SD 112.5s); and Radiologist C required 26.5s-249.3s (mean 136.2s, SD 63.3s). Overall, interpretation of an ABUS examination requires an average of 2.9 minutes of physician time (range, 26.5s-615.4s; SD 90.4s), which is less than the 20.8 minutes of physician time required for a HHUS examination.

CONCLUSION

Using ABUS for cancer screening in women with dense breasts requires less time than handheld ultrasound – 2.9 minutes versus 20.8 minutes. This suggests that ABUS can be efficiently integrated into clinical practice as an adjunct imaging technique for women with dense breasts.

KEYWORDS

3D ultrasound, automated breast ultrasound, ABUS, physician time, breast cancer.
Plk1 decreases DNA double strand break (DSB) formation during replication-stalling genotoxic stress

Polo-like kinase 1 (Plk1) is a regulator of the mitotic checkpoint, and is involved in adaptation, which is the progression of cells into mitosis with damaged DNA. Deregulation of Plk1 activity is linked to cellular transformation. Recent studies suggest Plk1 activity to be critical for resumption of cell cycle progression during recovery from DNA damage. However, the ability of Plk1 to affect the DNA damage response remains relatively unclear. The aim of the present study was to determine the ability of Plk1 to affect the DNA damage response in the face of different forms of DSB-inducing genotoxic stress. We employed the respiratory carcinogen, hexavalent chromium [Cr(VI)], the anticancer drug and topoisomerase II inhibitor, etoposide, as well as the oxidizer, H2O2. We have previously shown that Plk1 activation was sufficient to bypass the G2/M checkpoint in normal human lung cells (HLFs), in the presence of Cr(VI)-induced acute genotoxic stress. In the present study, we measured DNA DSB induction in HLFs by the respective genotoxins under the condition of Plk1 activation by using the comet assay and H2AX immunofluorescence staining. Transfection of HLFs with the constitutively active (c/a) Plk1 T210D mutant resulted in increased Plk1 protein expression 24h-48h post transfection. We used equitoxic concentrations of the different genotoxins and found that DNA DSBs increased > 2 fold after exposure to 3 μM Cr(VI), 12.5 μM etoposide, and 150 μM H2O2, respectively, and persisted for at least 4h. Consistent with DNA DSB formation, Cr(VI) exposure was associated with G1 arrest, at least at 4h, as determined by BrdU incorporation. Expression of the c/a T210D mutant increased Plk1 activity in vitro, and abrogated both Cr(VI) and etoposide-induced DNA DSBs as early as 30 min, and up to 4h post-treatment, in comparison to the vector control-transfected cells. In sharp contrast, treatment with 150 μM H2O2 induced a similar level of DNA DSBs in both the c/a T210D mutant- and vector-transfected cells. These data highlight the ability of Plk1 to enhance DNA repair uniquely under conditions of replication-stalling genotoxic stress. Given the documented roles of aberrant DNA damage response and Plk1 activation in cellular transformation, there is a critical need to define the molecular mechanism(s) by which Plk1 mediates decreased DNA DSBs after genotoxin exposure and delineate the pathways responsible for Plk1 activation. We postulate that the ability of Plk1 activation to abrogate DNA DSB formation after either Cr(VI) or etoposide exposure may occur at the expense of genomic stability. Supported by NIH grants CA107972 and ES017334 to SC and ES09961 and ES05304 to SRP and PhRMA foundation to GC.
Primary Gastric T-cell Lymphoma

Gastric lymphomas are mostly of B-cell in origin. Primary gastric T-cell lymphomas are rare and frequently associated with human T cell leukemia virus type 1 (HTLV-1) with poor prognosis. Herein, we present a case of primary gastric T-cell lymphoma that is HTLV-1 negative. The patient was a 68 year old African American man who presented with upper GI bleeding and anemia requiring multiple transfusions. Gastroendoscopy showed a large ulcer at the lesser curvature. A biopsy revealed diffuse lymphoid infiltrates consisting of predominantly medium to large atypical lymphocytes with moderate amount of pale cytoplasm, large nuclei, open chromatin and multiple nucleoli. The neoplastic cells were positive for CD2, CD3, CD4, CD5, CD7 and CD43, but negative for CD20, CD8, CD10, CD30, ALK1, EMA, TDT, CD56, with moderate to high proliferation index. PET CT scan demonstrated FDG avid gastric mass with adjacent suspicious lymphadenopathy. Serology testing for HIV and HTLV1 were negative. Partial gastrectomy with regional lymph node dissection confirmed a diagnosis of peripheral T-cell lymphoma, NOS, with one lymph node involvement. Primary gastric T-cell lymphoma is exceedingly rare and poorly characterized with challenging treatment. Further studies are necessary for more optimal and possibly targeted therapies.
miR-671-5p, a Novel Tumor Suppressor in Breast Cancer Progression

Our previous miRNA expression profiling study, using archived FFPE tissues, identified a set of miRNAs that are differentially expressed during breast cancer progression: Normal - Atypical Ductal Hyperplasia (ADH) - Ductal Carcinoma in situ (DCIS) - Invasive Ductal Carcinoma (IDC). Among the pool of deregulated miRNAs, miR-671-5p was found to be progressively downregulated during breast cancer development. This study shows that miR-671-5p consistently expresses low level in breast cancer cell lines, including MCF-7, Hs578T, T47D, SKBR3 and MDA-231, which indicates that miR-671-5p might function as a tumor suppressor in breast cancer initiation and progression. However, the exact mechanism is not clear. To test the effects of miR-671-5p expression on human breast cancer cells, we transfected miR-671-5p oligos and scrambled oligo mocks into human breast cancer cells, MCF-7 (ER+), MDA-231 (ER-), SKBR3 (ER-). We observed a significantly decrease in proliferation rate via MTT assay. These results indicate that miR-671-5p might serve as a potential therapeutic target in breast cancer. Further miRNA target prediction indicates that miR-671-5p targets genes and pathways involving cell proliferation, including ACVR2A (Wnt/β-catenin Signaling), APC (Basal Cell Carcinoma Signaling, Wnt/β-catenin Signaling), SERPINE2 (p53 Signaling), ADCY1 (Breast Cancer Regulation by Stathmin1), and CREB3L4 (ERK/MAPK Signaling, Estrogen-Dependent Breast Cancer Signaling). Further analysis of miR-671-5p in breast cancer cell metastasis and downstream targets validation are under way. In summary, we identified miR-671-5p as a potential tumor suppressor miRNA in breast cancer progression. It may serve as a therapeutic target for breast cancer.
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Should BRAF Mutation Status be used to Determine Extent of Surgery for Patients with Papillary Thyroid Cancer?

BACKGROUND

Papillary thyroid carcinoma (PTC) is a relatively indolent tumor and usually curable with surgical intervention; nonetheless, disease persistence and recurrence is common. Relevant to this, a growing body of research suggests the BRAF V600E mutation is associated with clinically aggressive disease (i.e. positive cervical lymph node metastasis) and should be used to determine extent of surgery. However, studies to-date have been mainly retrospective in design and do not include patients who have undergone routine central lymph node dissection (CLND) and are thus evaluable. Thus, we believe that insufficient information is available to make surgical recommendations based upon BRAF V600E mutation. To address this issue, we designed a retrospective study that included patients who had routine CLND and total thyroidectomy (TT) for PTC.

METHODS

Under IRB approval, we used identified consecutive patients at Johns Hopkins who had undergone TT and CLND for T1 or T2 disease. BRAF mutation status of each PTC tumor was determined retrospectively in fresh frozen or paraffin-embedded samples via colorimetric assay. Associations between BRAF mutation status and clinicopathologic features of PTC were then examined using chi-square tests.

RESULTS

Among 48 females and 12 males with a mean age of 44.9 years (SD = 11) and a mean tumor size of 2 cm (SD = 0.8), 42 (70%) had BRAF positive tumors and 18 (30%) were negative; 33 (55%) had lympho-vascular invasion and 27 (45%) did not; 12 (20%) had positive surgical margins and 48 (80%) did not; 35 (58%) had positive lymph nodes and 25 (42%) did not. BRAF mutation status was not significantly associated with any clinicopathologic features of PTC. Specifically, of the 42 BRAF positive tumors, 27 (64%) had lymph node metastases whereas 15 (36%) did not; of the 18 BRAF negative tumors, 8 (44%) had metastases whereas 10 (56%) did not (p = 0.153).

CONCLUSIONS

We believe that further investigation is necessary to assess whether aggressive clinicopathologic features of PTC are associated with BRAF V600E mutation. Because our results do not possess statistical power we will increase our cohort size until a power of 80% is achieved. Understanding the true relationship between BRAF V600E mutation and the clinicopathologic features of PTC will have a significant impact upon the surgical recommendations for patients with this disease.
The Pathology and Epidemiology of Thymoma: An Analysis of 2,409 Cases from the SEER Database

INTRODUCTION

The biology and clinical behavior of thymic tumors are governed by histomorphometric patterns, tumor grade, and stage. Most studies utilize limited data for tumor evaluation and prognosis. We have investigated the NCI’s Surveillance, Epidemiology, and End Results (SEER) database to identify demographic and clinical prognostic factors.

METHODS

Data were obtained from NCI’s SEER program and include information from Registry 17 (1973-2007) and Registry 9 (1973-2007). Cases were compared by linear plots of incidence, age of diagnosis, relative Kaplan-Meier survival rates, and frequency density, and by linear and log-log plots of the age specific incidence rates. World Health Organization (WHO) Types A, AB, B1, B2, B3, and C were considered. Rates are expressed as number of cases per 100,000 persons.

RESULTS

Thymomas affect men at a greater rate than women (M:F=0.22:0.17). Thymomas have increased in incidence continuously over thirty-four years (1973-2007) with a doubling in incident rate (0.12 to 0.27). Thymic carcinomas (WHO Type C) have increased at a similar rate. Log-log plots of age versus incidence showed near-parallel slopes of thymic histologic types, suggesting a common pathogenesis for all thymomas. Frequency density plots showed that all thymomas (low grade, high grade, and carcinoma) have near-identical distributions. All thymomas appear to have an incidence rate peak in the 8th decade. Relative Kaplan-Meier survival calculations demonstrated that 5-year survival rates can be stratified into three groups: I. Type A, AB, B1 (85%); II. Type B2, B3 (79%); and III. Type C (49%).

CONCLUSIONS

Thymic tumors are increasing as the age of the population increases, although there may be other factors generating the increase in incidence. All thymomas have similar age frequency distributions despite the differences in tumor histologic patterns. Results of survival analysis suggest that a more limited stratification of tumor histologic patterns would best define prognostic groups. Except for survival, thymic carcinomas have the same epidemiologic patterns as other thymic tumors.
Protein profiling of pediatric diffuse intrinsic pontine gliomas

BACKGROUND
Gliomas comprise approximately 60% of all pediatric brain tumors and 10-15% of these are located within the brainstem. A subset of high grade brainstem gliomas that typically manifest during childhood are known as diffuse intrinsic pontine gliomas (DIPG). Radiation therapy of DIPGs provides transient management, however they are treatment refractory with median survival shorter than 1 year. Recent research indicates stereotactic biopsy of DIPGs is a relatively safe procedure, and thus interest in tissue biopsy has gained resurgence. Previous unpublished data completed on CSF specimens implicates a number of dysregulated proteins unique to DIPGs. The purpose of this study is to generate and analyze the complete protein profile of frozen control and tumor specimens obtained from patients with DIPGs as well as other cranial tumors.

METHODS
Frozen brainstem tumor specimens from patients were compared to control brainstem or frontal lobe sections. Specimens included DIPG (n=11), non-brainstem tumors (n=5), brainstem controls (n=11), and frontal lobe controls (n=1). Total protein was extracted using RIPA buffer. Extracted proteins were separated using 1D SDS-PAGE followed by in-gel tryptic digestion. MS/MS quantitative proteomic analysis was completed using LTQ-Orbitrap-XL. Bioworks software was used to query MS/MS against Uniport Swiss-Prot human database followed by protein and pathway analysis using ProteoIQ and Ingenuity Pathway Analysis software, respectively.

RESULTS
Isolated peptides were identified and unsupervised clustering showed that DIPG specimens exhibit a unique pattern of protein expression when compared with non-brainstem tumors and controls. Pathway analysis indicated tumor-associated pathways including glioma formation, cell migration, or response to oxidative stress.

CONCLUSIONS
Over 30 years of clinical efforts in treating children with highly lethal DIPGs have resulted in little progress. Furthermore, a lack of specific diagnostic techniques makes management and counseling for patients difficult. In this study, we seek to understand the biology of the tumor and its underlying molecular pathways by generating the complete protein profile of frozen specimens. To the best of our knowledge, this is the first comprehensive protein profiling of frozen DIPG specimens. Validation of the observed protein dysregulation and comparison to our recent CSF protein profiling of these patients is underway and will be valuable for identification of novel biomarkers that could be used for disease management and targeted therapeutics.
GW Cancer Institute Results from the 2010 LIVESTRONG Survey for People Affected by Cancer

BACKGROUND

There are currently more than 12 million cancer survivors in the US, and many of these individuals face late and long-term effects of cancer and its treatment. Little is known about DC-area survivors regarding what effects survivors are most concerned about and whether these concerns are being addressed.

METHODS

The GW Cancer Institute recruited participants for the 2010 LIVESTRONG Survey for People Affected by Cancer. The electronic survey included questions regarding the physical, emotional, and practical concerns affecting cancer survivors after treatment ends. There were 37 total respondents from GW: 23 post-treatment survivors, 1 patient in treatment, and 13 caregivers. The majority identified as white females. All had health insurance and the median income level was $101,000-$120,000.

RESULTS

Seventy-eight percent of the survivor respondents reported one or more physical health concern; the most common physical health concerns were concentration, energy, and sexual functioning and lymphedema (tied). Seventy-four percent reported at least one emotional concern; the most common emotional concerns were worry, grief and identity problems, and concerns about appearance. At least one practical concern was reported by 57%; employment and finances were most common. GW ranked very high for health care professional interactions for addressing health-related questions, providing emotional attention, helping patients understand how to take care of their health, and patient involvement in care decisions. Respondents indicated that feelings of uncertainty about their health and care were common. Survey results suggest satisfaction in addressing information needs during treatment; survivors indicated information needs after treatment, especially information about late effects.

CONCLUSIONS

Similar to national trends, GW patients have physical, emotional and practical concerns after treatment ends; many patients reported having their needs met. Understanding the specific physical, emotional, practical, and informational needs of GW cancer survivors will help GW better address and be responsive to those needs.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Can magnetic resonance image-targeted prostate biopsy diagnose clinically significant prostate cancer with greater efficiency than transperineal template biopsy?

OBJECTIVE/BACKGROUND

There is much interest in improving the performance of prostate biopsy from the current standard of transrectal cores taken with ultrasound guidance alone. One approach is to do a Transperineal Template Prostate Biopsy (TPB) using a greater sampling density than the usual transrectal approach. An alternative approach is to use MRI-targeted prostate biopsy to limit sampling to areas suspicious of cancer depicted on multi-parametric MRI (mpMRI). A cohort of men who underwent both TPB and MRI-targeted biopsy is represented. Both approaches are compared for detection rates of clinically significant disease and the number of cores taken to give a diagnosis of clinically significant prostate cancer. MRI-targeted biopsy may confer similar accuracy of TPB with reduced sampling burden.

METHODS

115 men with a raised PSA and an abnormality detected on mpMRI underwent targeted biopsy followed by TPB. The detection rates for clinically significant cancer were evaluated, with a ≥ 4mm cancer core length and any Gleason pattern 4 defining significance.

RESULTS TO DATE

Mean age was 63.5±7.5, presenting PSA was 7.5±4.2ng/ml, mean number of targeted cores per patient was 4.9±2.3 and mean number of TPB cores was 35.6±19.9. The sampling density for TPB was 0.88 +/- 0.55 cores/ml.

TPB identified clinically significant cancer in 70/115 (61%) men and insignificant cancer in 17/115 (15%) at a sampling efficiency of 47 cores per diagnosis. MRI-targeted biopsy identified clinically significant cancer in 68/115 (59%) and clinically insignificant in 8/115 (7%) at a sampling efficiency of 7.4 cores per diagnosis. Sixteen clinically significant cancers were missed by the MRI-targeted biopsy and 14 clinically significant cancers missed by TPB. MRI-targeted biopsy identified 5 clinically insignificant cancers not detected by TPB in contrast to TPB that identified 14 clinically insignificant cancers not detected by MRI-targeted biopsy.

CONCLUSIONS

MRI-targeted biopsy has a similar detection rate to TPB for clinically significant prostate cancer. This strategy is also more likely to overlook clinically insignificant prostate cancer, with a considerably lower sampling burden.
Radiosensitization of Melanoma Cell Lines Using the Mutant B-Raf Inhibitor GSK2118436

Objectives: Melanoma is an aggressive cancer that has an increasing incidence in the United States. Patients with metastatic melanoma commonly develop brain metastases. An activating valine-glutamate substitution at position 600 of the B-raf protein has been implicated in approximately 50% of melanoma cancers. The B-raf protein is a serine/threonine protein kinase of the RAS-RAF-MEK-MAPK signaling pathway involved in growth and proliferation. GSK2118436 is a molecular inhibitor that selectively binds and blocks the activity of mutant B-raf proteins. Early clinical trials show that GSK2118436 may control and reduce brain metastases from melanoma. The effects of combinatorial treatment of melanoma brain metastases with GSK2118436 and ionizing radiation therapy are currently unknown. The combined therapy could be toxic, neutral, additive or synergistic. By determining if GSK2118436 can increase the sensitivity of radiation resistant melanoma cells to ionizing radiation treatment, this study assesses the capability of GSK2118436 to synergistically kill or radiosensitize human B-raf mutant melanoma cell lines.

METHODS

Clonogenic survival assays were performed to assess in vitro cell survival following increasing doses of radiation (0-8 Gray) using four melanoma cell lines: A375, WM2664, WM35, and SKMEL5. Radiosensitization of cell lines was determined by comparison of survival with and without the B-raf inhibitor, GSK2118436. Molecular inhibition of mutant B-RAF was confirmed by immunoblot analysis.

RESULTS

BRAF mutant melanoma cell lines showed varying radiosensitivities to radiation treatment. The radiosensitivity was determined with cell lines listed in order of decreasing radiosensitivity: WM2664 > SKMEL5 > A375 > WM35. WM2664 was the most sensitive to radiation with the highest survival fraction after 2 Gray (SF2). WM35 was the most resistant to radiation with the lowest SF2 value. A375 and WM35 were selected as candidates for examining radiosensitivity effects of combinatorial GSK2118436 and radiation therapy. The survival fraction decreased significantly with low dose GSK2118436 combination in the radiation resistant cells (WM35). A375 are semi-radiation sensitive cells and the response to B-raf inhibitor was not as dramatic as seen in the radioresistant line WM35.

CONCLUSIONS

The inhibitor GSK2118436 increases radiation sensitivity in the radiation resistant, mutant B-raf melanoma cancer cell lines. Our results confirm that melanoma cell lines demonstrate variable sensitivity to radiation therapy. More radioresistant cell lines were more effectively radiosensitized by inhibition of mutant B-raf by GSK2118436. Further in vivo validation is ongoing. Our data suggests a role for the use of GSK2118436 in combined treatment with radiation for patients with B-raf mutated melanoma brain metastases.
Breast conservation surgery followed by radiation is the standard of care for patients with early stage breast cancer. Complications related to radiation treatment can range from mild skin changes to debilitating and disfiguring reactions that require further treatment. Severe fibrosis can occur in patients with collagen vascular disease, higher total dose or boost radiation, and obesity. Calcifications can develop following radiation and are frequently due to fat necrosis. The less common combination of fibrosis with calcifications can mimic cancer on physical examination and mammography, posing a challenge to clinicians caring for these patients.

We discuss the case of a 56-year-old woman who presented with suspicious micro-calcifications and progressive fibrosis 4 years following lumpectomy and radiation therapy for early stage breast cancer. Minimally invasive and subsequent excisional biopsies were all negative for recurrent malignancy. The patient ultimately elected to have a mastectomy due to worsening mammograms, extensive fibrosis, and the disfigurement that occurred as a result of this complication and the multiple biopsies.

This report presents a rare complication following breast conservation therapy for breast cancer. Although ultimate pathology may be benign, our case highlights the importance of ruling out recurrent malignancy in patients previously treated for breast cancer who present with suspicious imaging. A review of the relevant literature is included in this case report.
Breast-specific gamma imaging for detection of breast cancer in dense versus non-dense breasts

Objectives
The purpose of this study is to evaluate the sensitivity of BSGI for the detection of breast cancer in dense versus non-dense breasts.

Materials & Methods
This is a retrospective study of 341 women with biopsy-proven breast cancer diagnosed from January 2004 to August 2009 who underwent BSGI prior to surgical excision. Patients with breasts described as almost entirely fat (BIRADS 1) or scattered fibroglandular densities (BIRADS 2) were classified as non-dense while those described as heterogeneously dense (BIRADS 3) or extremely dense (BIRADS 4) were classified as dense. BSGI examinations exhibiting focally increased radiotracer uptake in the area of biopsy-proven cancer were considered positive according to BSGI reports in the medical record. The sensitivity of BSGI was calculated using Microsoft Excel (2003, Microsoft Corporation, Redmond, WA). Between-group differences were evaluated statistically using the Student t test for continuous variables and the χ2 test for categorical variables, with P < 0.05 considered statistically significant.

Results
The overall sensitivity of BSGI for breast cancer detection was 95.4%. Positive BSGI examinations were present in 136 of 142 non-dense breast cancers and 195 of 205 dense breast cancers for sensitivities of 95.8% and 95.1%, respectively. There is no significant difference in BSGI breast cancer detection and parenchymal breast density (P = 0.776).

Conclusion
BSGI has high sensitivities for the detection of breast cancer in women with dense and non-dense breasts, and is an effective adjunct imaging modality in women regardless of breast density.
# Potential Role of Nitric Oxide in Chromium-Induced Lung Carcinogenesis

## Background

Certain hexavalent chromium [Cr(VI)] compounds are well-established human respiratory toxins and carcinogens of occupational and environmental relevance. Our recent studies have shown that intranasal (IN) exposure of Balb/c mice to particulate zinc Cr(VI) compounds leads to pronounced innate inflammation in the lung, which we postulate plays a significant role in pulmonary tumorigenesis. Nitric oxide (NO) has been shown to be induced via inflammatory response mediators, and has been implicated in the progression of different cancers, including lung. Moreover, NO-induced tumor invasiveness has been correlated with enhanced matrix metalloproteinase (MMP) expression in lung tumor cell lines. Of particular relevance to the present study is the finding that in vitro exposure of human lung cells to Cr(VI) in culture led to increased NO production. The aim of the present study was to explore the role of NO in chromium-induced lung tumorigenesis.

## Methods

BALB/c mice received weekly IN delivery of either saline or 10 ug particulate basic zinc chromate, which is an intermediately water soluble chromate typically encountered in mining/chromate production facilities and which is also present as an environmental atmospheric contaminant in urban areas surrounding ferrochrome production facilities. After 9 weeks, immune cells, cytokines, NO, MMPs and pathologic features of lung injury and inflammation were measured in airway lavage fluid and lung tissue, at both 24h after the final Cr(VI) dose, as well as 1 week later.

## Results

As previously shown, repetitive Cr(VI) exposure induced a neutrophilic inflammatory airway response 24h after treatment. Neutrophils were subsequently replaced by increasing numbers of macrophages 1 week after treatment. Peribronchiolar inflammation was observed in chromate-exposed mice, and was accompanied by a 100-fold increase in pro-MMP9 release into the airways. Notably, airway NO was significantly increased ~ 1.9 fold in Cr(VI)-exposed mice as compared to their saline-treated counterparts at both time points following final exposure. Moreover, immunoreactivity of induced nitric oxide synthase (iNOS) was markedly increased in airways exposed to Cr(VI), with staining localized to infiltrating immune cells.

## Conclusion

Repetitive exposure to particulate chromate induces an inflammatory environment in the lung, accompanied by enhanced NO production, which we postulate may promote Cr(VI) carcinogenesis.
Role of the inflammasome complex in Cr(VI)-induced lung injury and inflammation

BACKGROUND

Certain particulate hexavalent chromium [Cr(VI)] compounds are human respiratory carcinogens that release genotoxic soluble chromate, leading to fibrosis, fibrosarcomas, adenocarcinomas and squamous cell carcinomas of the lung. While considerable information exists regarding Cr(VI) genotoxicity in cell culture, the mechanisms by which Cr(VI) causes lung injury and carcinogenesis in vivo are still unknown. We postulate that early inflammatory processes and mediators may contribute to the etiology of Cr(VI) carcinogenesis. We have previously established that intranasal (IN) particulate Cr(VI) administration in Balb/c mice induced a pronounced innate inflammatory response in the lung. Our present aim was to directly test the contribution of inflammasome-mediated inflammatory processes to chromate-mediated lung cancer development.

METHODS

We used WT and inflammasome-deficient (ASC knockout) BALB/c mice for weekly IN delivery of either saline or 10 ug particulate basic zinc chromate, which is an intermediately water soluble chromate typically encountered in mining/chromate production facilities and which is also present as an environmental atmospheric contaminant in urban areas surrounding ferrochrome production facilities. After 9 weeks, immune cells, cytokines, MMPs and pathologic features of lung injury and inflammation were measured in airway lavage fluid and lung tissue.

RESULTS

Inflammasome-deficient mice exhibited a markedly reduced number of airway leukocytes in response to Cr(VI) challenge when compared to their WT counterparts, which was particularly evident for macrophages. Moreover, the Cr-induced increase in airway levels of IL6 (8-fold), CXCL/KC (3-fold), as well as pro-MMP9 (100-fold) was significantly attenuated in the inflammasome-deficient mice. In contrast, histological examination of lung tissue in animals challenged with chromate revealed a similar increase in peribronchiolar inflammation in both WT and ASC-/- mice, suggesting that Cr-induced lung inflammation may involve ASC-dependent and independent mechanisms, and that tissue infiltration may be less impacted by ASC-dependent mechanisms.

CONCLUSION

Particulate chromate is a potent inducer of inflammatory responses in the lung, mediated in part through the inflammasome complex. We postulate that these early inflammatory processes may contribute to the etiology of Cr(VI) carcinogenesis. The findings may also be relevant to other lung particulates that induce injury and cancer. Supported by NIH grants CA107972 and ES017334 to SC and ES017307 to SRP.
B7-H1 expression in lung cancer is associated with active PI3K pathway signaling: a possible link of immune escape and oncogenesis

**BACKGROUND**

Lung cancer has the highest mortality rate in the United States and currently there are 90,000,000 past or present smokers at risk for developing lung cancer. With only a 16% 5 year survival rate, new therapies are desperately needed. Currently a major focus of therapeutic development is limiting tumor-mediated immunosuppression, a mechanism of which includes the immunosuppressive ligand B7-H1. B7-H1 is over-expressed and linked to poor prognosis in several human epithelial cancers, including non-small cell lung cancer. Recently, B7-H1 expression has been linked to the loss of the tumor suppressor PTEN and subsequent activation of the PI3K pathway in glioma, breast and prostate cancer. As lung cancer is strongly associated PI3K pathway activation, we hypothesize that these tumors are an ideal model to further investigate the relationship between oncogenic signaling and B7-H1-mediated immunosuppression.

**METHODS**

We investigated the active PI3K signaling and B7-H1 link by using murine cell lines generated from a tobacco carcinogen NNK-induced mouse model of smoker’s lung cancer and human lung cancer cell lines. Small molecule pathway inhibitors targeting PI3K, AKT and mTOR were used to treat cell lines highly expressing B7-H1. Addition of EGF and targeted siRNA to PTEN were used on cell lines with low B7-H1 expression. In vivo B7-H1 expression was examined by immunohistochemistry of lung tumors from multiple models of murine lung cancer.

**RESULTS**

B7-H1 is expressed at varying levels in both human and NNK-induced mouse lung cancer cell lines. Cell lines with a high level of B7-H1 protein could be decreased with each pathway inhibitor, the most rapid and potent of which was seen with rapamycin mediated mTOR inhibition. Basally low B7-H1 expressing cell lines could up-regulate the protein with PI3K pathway activation through PTEN loss or EGF addition. Immunohistochemistry showed B7-H1 in vivo expression in syngenic sub-cutaneous tumors of NNK-induced lung cancer cell lines and in lung tumors induced by NNK administration or somatic mutation of KRas and EGFR.

**CONCLUSIONS**

We provide evidence that B7-H1 expression in both human and murine lung cancer is linked to PI3K pathway activation in vitro. In both carcinogen induced and genetically engineered models of murine lung cancer we demonstrate that B7-H1 is expressed in vivo. These observations describe a valid system to further explore the link between lung tumor oncogenic changes and the development of an immunoresistant phenotype, ultimately in efforts for identifying rational therapeutic combinations.
The glucagon receptor functions as a tumor suppressor that is lost in advanced-stage hepatocellular carcinoma

BACKGROUND
The glucagon receptor (GR) is an essential metabolic regulator and contributor to cell homeostasis. Glucagon signaling through the GR also tightly controls cell proliferation and migration genes. Abnormalities in this signaling network are commonly observed in disease states that include diabetes, pancreatitis, and steatosis. Interestingly, elevated circulating glucagon levels, as commonly seen in hyperglycemic patients, have been cited as a risk factor for pancreatic, liver, and colon cancers. However, the GR’s mechanism of action in cancer prevention remains unknown. The purpose of these studies has thus been to evaluate the GR’s function as a tumor suppressor in hepatocellular carcinoma (HCC).

METHODS
Hep3B cell lines stably expressing the GR or a GFP-tagged empty vector were constructed using a pMX retrovirus vector and grown from a single colony; cell lysates were extracted to analyze gene expression through quantitative RT-PCR. GR expression in primary patient tumors was evaluated by immunohistochemistry and immunocytochemistry. Site-specific antibodies and/or siRNA were directed against proteins involved in the hypothesized signaling pathway to determine the mechanism of glucagon-mediated signaling. Invasion assays were conducted using Matrigel-coated chambers containing epidermal growth factor, γ-aminobutyric acid (GABA), or veratridine.

RESULTS
There is gradual GR loss as cancer progresses, with little detectable GR in primary tumors of advanced-stage HCC. GR signaling occurs through a PKA and c-Raf-1-mediated mechanism to regulate transcription of migration and invasion genes. Furthermore, glucagon stimulation of HCC cell lines stably expressing the GR leads to differential changes in ion channel expression. The activation of several ion channels, most notably voltage-gated and ligand-gated cationic channels, has been previously implicated in the metastatic potential of solid tumors. HCC invasive potential was inhibited by pharmacologically targeting these channels, specifically sodium and chloride channels.

CONCLUSION
We have shown that GR expression plays a critical role in HCC progression. The up-regulation of cationic channel and down-regulation of anionic channel gene expression that occurs following GR loss can be employed to inhibit HCC invasion as the tumor suppressor capabilities of the GR are lost. These findings suggest that ion channel activation may play a critical role in preventing liver cancer metastasis.
Delineation of the Genome-wide Recruitment of Hepatitis B Virus Trans-activator Protein HBx, in Primary Hepatocytes and Liver Cancer Cells

BACKGROUND

HBx, a known viral trans-activator protein of the Hepatitis B virus, has been shown to interact with NF-kB/RelA and Metastasis Tumor Antigen 1 (MTA1) to target the host’s genome, to alter cellular gene expression which could contribute to the development of Hepatocellular carcinoma (HCC). Here, we defined the genome-wide recruitment of HBx and its dependency on the master cellular router and coregulator, MTA1, to target cellular genes, which in-turn, may be important in the process of HCC development.

METHODS

Lentiviral vectors containing control, HBx, or mutant (devoid of the RelA binding motif) HBx sequences were used to transduce primary human hepatocytes (PHH) and liver cancer cells (HepG2) and select samples were subjected to MTA1 siRNA to knock-down the expression of MTA1. Chromatin Immunoprecipitation (ChIP) was used to isolate genome-wide chromatin which was bound by HBx in various treatment conditions. Deep sequencing was completed by 60 bp reads on an Illumina platform. Datamining with Avadis NGS, Ingenuity Pathway Analysis and the UCSC Genome Browser, was completed to reveal and analyze genome-wide recruitment and specific gene targets.

RESULTS

The genome-wide recruitment of HBx is altered by changing the involvement of NF-kB/RelA and MTA1, which is also distinct between normal and cancerous liver cells. HBx recruitment increases in PHHs as the involvement of both cellular factors is reduced. Characterizations were completed to reveal overall recruitment patterns as well as recruitment patterns to top unfiltered targets, to all genes targeted at promoter/upstream regions, to genes with proximity to chromatin marks, and those related to gene expression and cancer. The results of these analyses provide a comprehensive, global view of HBx recruitment, dependent on and independent of NF-kB/RelA and MTA1.

CONCLUSIONS

These results reveal that NF-kB/RelA and MTA1 play central roles in the genome-wide recruitment of HBx. Reduced involvement of these factors in PHHs increased recruitment to total genes, significant regions of genes, cancer related genes and gene expression and regulation related genes. We show that HBx targets different sets of genes in primary hepatocytes and liver cancer cells. These targets include homeobox transcription factors, genes associated with RNA Polymerase II, and genes involved in development. These findings suggest that NF-kB/RelA and MTA1 play important, distinct roles in normal as well as cancerous liver cells and that these factors may alter the ability of the viral protein HBx to target genes and change gene expression which may contribute to the development of cancer.
Racial Disparity in Hepatocellular Carcinoma in Presentation, Treatment, and Mortality: Analysis of a Nationwide Inpatient Database

BACKGROUND
Our objective was to evaluate the impact of patient race upon presentation, treatment, and post-treatment outcome of hepatocellular carcinoma (HCC).

Methods: University Health Consortium is a nationwide clinical and administrative database compiled from 42 states representing 90% of the non-profit academic medical centers. Adult admissions with primary discharge diagnoses of HCC in 2002-2011 were identified using International Disease Codes 9th edition. Information about demographics, liver decompensation, comorbidities, metastases, inpatient death, geographic location, and treatment allocation were included in a multivariate model predicting metastasis at first admission (presentation) and treatment allocation. Propensity scores for receiving each treatment were calculated and included in a model predicting inpatient mortality (post-treatment outcome). Results are presented as odd ratios with their corresponding p values.

RESULTS
We identified 27,741 patients with a median age of 60.8 years. The population was composed of Caucasians 53.9%, African-Americans (AA) 16.2%, Hispanic 9.3%, Asians 10.7%, and others 9.9%. Compared to Caucasians, AA (1.2, p<0.001) and Asians (1.23, p=0.001) were more likely to present with metastasis and AA were less likely to receive invasive procedures: transplant (0.46, p<0.001), resection (0.53, p<0.001), ablation (0.67, p<0.001). Compared to Caucasians, Asians were as likely to receive transplant and ablation and more likely to receive resection (1.35, p<0.001). Compared to Caucasians, AA (1.62, p<0.001) and Asians (1.27, p<0.001) had higher inpatient mortality from HCC in univariate analysis. However, after controlling for the aforementioned confounders and treatment allocation factors using propensity scores, AA have lower (1.29, p<0.001) mortality than Asians (1.63, p<0.001).

CONCLUSION
Compared to Caucasians, Asians and AA presented with more metastasis, yet AA did not receive as many invasive treatments as Asians. In addition, AA and Asians had a higher inpatient mortality than Caucasians. While we observed a difference in mortality that favors Asians when compared to AA on a univariate level, once the disparity in treatment allocation was evaluated using propensity score, the mortality trend reversed in favor of AA. More importantly, after using propensity scores to mimic randomization of treatment options, inpatient mortality (62% excess in AA compared to Caucasians) was reduced to 29% indicating that the observed disparity in mortality might extend beyond disproportionate treatment allocation. Further research should be directed towards understanding the basis of this significant racial disparity.
CAP as an alternative for cancer therapy

BACKGROUND

CAP (cold atmospheric plasma) is a technology which is based on quasi-neutral ionized gas (plasma at low temperatures) which is being evaluated as an alternative or addition to existing cancer therapies. A recent study shows that CAP treatment can cause a significant reduction in tumor size in vivo. Thus the purpose of this study is to begin to identify the mechanism by which cancer cells are killed by CAP.

METHODS

The studies were performed on normal and transformed epithelial cells. The impact of CAP on cells was evaluated through cell migration studies (microscopy time lapse studies of cells), cell cycle studies using flow cytometry, and viability studies using MTT assays. In addition, cells were synchronized to the same stage of the cell cycle using nocodazole and DNA damage after CAP treatment assessed by evaluating expression of the S-phase damage reporter phospho-histone yH2A.X.

RESULTS

It was found that normal and transformed cells respond differently to CAP treatment. Using a mild CAP treatment, it was observed that migration of normal cells was reduced ~30% (p<0.001). While aggressive carcinoma cells showed also decreased their migration rates after CAP (~20% with p<0.001), less aggressive papilloma cells did not (p>0.05). Flow cytometry studies show that CAP induces a robust G2/M-cell cycle arrest in both types of carcinoma (double fold increase in G2/M phase in ~24 hours after CAP treatment). Normal epithelial cells showed a more modest cell cycle arrest.

CONCLUSIONS

Experiments show a G2/M arrest is induced by CAP treatment in two different types of cancer cells. These data support the hypothesis that the increased sensitivity of cancer cells to CAP treatment is caused by differences in the distribution of cancer cells and normal cells within the cell-cycle. Because more cancer cells are actively proliferating, more are in the S-phase of the cell cycle. Data show that cells in the S phase are more vulnerable to CAP treatment.”
Cold Plasma Therapy as a Novel Chemotherapeutic Strategy

BACKGROUND

Plasma, the fourth state of matter, is composed of partially ionized gas containing electrons, excited molecules, free radicals and ions.1 Historically, plasma could only be produced at high temperatures or in vacuums, however, recent advances in plasma physics have led to the production of plasma at room temperature.2,3 While theoretically any gas or mixture of gases can be used, our group used Helium due to the advantages of it being monatomic and chemically inert. Cold plasma treatment (CPT) can potentially be used in cancer therapy by generating reactive ion species that may induce tumor cell apoptosis. Our initial studies demonstrated efficacy in killing tumor cells in both in vitro and in vivo mouse models of neuroblastoma. We therefore sought to advance these findings by evaluating the effects of cold plasma in human neuroblastoma and normal fibroblast cell lines.

METHODS

IMR-32 human neuroblastoma cells and human fibroblasts (ATCC 895.sk) were administered a constant dose of CPT for 30, 60 and 120 seconds respectively. Cell apoptosis was analyzed by flow cytometry using annexin V-FITC and 7-AAD staining at four different time points after CPT treatment: immediately, 24 hours, 48 hours, and one week.

RESULTS

CPT of neuroblastoma cells induced a three to six-fold increase in apoptosis compared to controls. CPT induced a dose-response effect in the tumor cells decreasing cell viability by up to 98 percent. Conversely, CPT had little effect on human fibroblasts; these cells maintained their viability compared to untreated controls.

CONCLUSION

CPT can induce apoptosis mediated cell death of human neuroblastoma cells, while normal human fibroblasts remained largely unaffected by treatment. Cold plasma therefore represents a potential emerging adjunct in cancer therapy, with selective and effective in vitro targeting of human neuroblastoma. The mechanism of this tumor selectivity needs to be elucidated, however it is believed to be mediated by the generation of reactive oxygen species.

SOURCES

Primary Cutaneous CD30-Positive Large T-Cell Lymphoma in an 80-Year-Old Man: A Case Report

Primary cutaneous CD30-positive large cell lymphoma (CD30+ PCLCL) is a rare subtype of cutaneous T-cell lymphoma (CTCL) that can present in a variety of ways. We report a patient with a three-month history of an enlarging, exophytic mass with two smaller satellite lesions on the left forearm. Biopsy of the skin stained positive for CD30, and, after thorough systemic evaluation, a diagnosis of CD30+ PCLCL was made. When PCLCL is suspected, it is important to perform immunohistological studies for CD30 types and conduct a thorough workup to rule out systemic LCL. These measures will reduce the use of unnecessarily aggressive chemotherapy regimens for CD30+ PCLCL, an indolent disease with a favorable prognosis."
Sickle Cell Disease (SCD) affects millions of people globally and over 70,000 in the United States. The severity of the disease ranges from relatively asymptomatic states to very severe requiring hospitalization; the severe phenotype is associated with high morbidity and early mortality. Improvements in the quality of care and the development of more effective maintenance therapies have improved the quality and longevity of life for patients with SCD with access to state-of-the-art health care. However, the only available curative therapy for SCD is hematopoietic stem cell transplant (HSCT). Current barriers to stem cell transplant include: patient selection, identification of a matched donor, availability of the donor, geographic location/economy, transplant complications, and late effects of transplant. As HSCT (in particular matched related donor bone marrow transplant) for SCD patients is becoming more successful, there exists a nearly universal consensus that there is a need for more donors. This study was designed as a cross-sectional chart review of all sickle cell patients at Children’s National Medical Center (CNMC) who have undergone HLA-typing. This review compared patient HLA typing with available donors in the National Marrow Donor Program (NMDP) as well as international and cord blood registries to evaluate how many 8/8 and 7/8 HLA matched bone marrow donors and 6/6 and 5/6 HLA matched cord blood donors at the allele level were found, and whether these donors were available to donate. Currently half of the expected data has been collected and preliminary results have yielded a combined (8/8, 7/8, 6/6, and 5/6) match rate of less than 30%.
The Role of the BP1 Homeobox Gene in Triple Negative Breast Cancer

**BACKGROUND**

Triple negative breast cancers (TNBC) lack the expression of ER, PR and HER2 receptors and are usually high grade tumors. Thus, targeted treatments against nuclear ER and PR or the surface receptor HER2 are not effective. We are studying the Beta Protein 1 (BP1) gene, which we cloned and showed is activated in 80% of invasive ductal breast cancers; its expression correlates with breast cancer progression and invasion. Since BP1 mRNA and protein are highly expressed in ER and PR negative and clinically aggressive tumors, we hypothesize that BP1 may be activated in TNBC. The main objective of our project is to evaluate the role BP1 in TNBC.

**METHODS**

We have characterized six TNBC cell lines and one non-TNBC cell line for expression of BP1 and other previously determined BP1 targets. Analysis of mRNA and protein expression was performed using qPCR and Western blot analysis, respectively. One TNBC cell line, HCC38, expressing high levels of BP1 mRNA and protein was selected for RNAi-mediated knock down (siRNA) to investigate the changes in global gene expression resulting from reduced expression of the BP1 gene. To delineate pathways in TNBC cells dysregulated in the presence of high BP1 levels, we extracted RNA from eight cell lines for microarray analysis.

**RESULTS**

All of the TNBC cells have at least 2.8-fold more BP1 protein (pBP1) than non-TNBC cells, suggesting there may be higher pBP1 in TNBC tumors than in non-TNBC tumors. Knock-down of BP1 in HCC38 cells was performed at 72 hrs, 90% reduction of BP1 mRNA was observed with 90 pmol of siRNA duplex. The effect of BP1 knockdown on other genes is under investigation. Gene expression microarrays revealed significant up/down regulation of several genes, including MYC and EGFR, in TNBC cell lines as compared to non-TNBC cell lines. The IL-6 gene was upregulated in cells overexpressing BP1 whether TNBC or non-TNBC. Microarray results will be verified by qPCR and Western blot analysis. Studies are underway to establish the mechanism by which these pathways are regulated by BP1.

**CONCLUSIONS**

BP1 may upregulate important oncogenic pathways in TNBC and thus could be a valuable molecular marker and therapeutic target in this aggressive form of breast cancer.
Healing Pathways: Art Therapy for American Indian Cancer Survivors

There is a paucity of research addressing quality of life factors for American Indian and Alaska Native cancer survivors. Complementary forms of therapy, such as art therapy, are beginning to address quality of life factors through the “healing” arts for cancer survivors. The purpose of this mixed methods pilot was to explore the effects of culturally-relevant art interventions on stress reduction for American Indian cancer survivors and their family members. Forty six adult participants attended one of three workshops held within two settlements of the Coharie tribe and one southeastern urban tribal center. The data collected consisted of a pretest and posttest State-Trait Personality Inventory (STPI) and artwork resulting from 3 directed interventions. The artwork was analyzed using qualitative coding methods; however, the scores from the STPI were inconclusive because the inventory was determined to be culturally biased. While statistical significance was not achieved, the findings from qualitative coding reinforced a Native concept of wellness focusing on the complex interaction between mind, body, spirit, and context. This pilot study also demonstrated how a community-driven approach was instrumental in the development of the overall workshop format. An expansion of the pilot study is also presented with preliminary results available in 2012.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Distribution of M1 and M2 macrophages in different locations in carotid plaques

BACKGROUND

Atherosclerosis affects the vascular system and is the leading cause of death in the United States. Rupture of the atherosclerotic plaque is the major cause of acute coronary syndrome. Macrophages play a large role in atherosclerosis because they are responsible for the uptake of lipids from the plaque and weaken the stability of the plaque by secreting matrix metalloproteinases. Two major macrophage subtypes have been identified: M1 and M2 macrophages. Generally, M1 macrophages are pro-inflammatory, having increased secretion of proinflammatory cytokines to further augment cell-mediated adaptive immunity. Contrastingly, M2 macrophages thought to be anti-inflammatory, playing a key role in wound healing as well as tissue remodeling. Currently, the distribution of M1 and M2 macrophage in different locations in carotid plaques is unknown. The purpose of this study was to assess the distribution of M1 and M2 macrophage in different locations in carotid plaques.

STUDY DESIGN

Carotid plaque samples were obtained during carotid endarterectomy (N = 19). Each sample was classified using the American Heart Association (AHA) classification. Each sample was divided into upstream, central, downstream and normal regions (if a normal region was able to be collected). Infiltration of M1 and M2 macrophages was investigated by immunohistochemical staining with antibodies against receptors and cytokine markers. M1 receptor marker was anti-CD40, and the M1 cytokine marker was TNF alpha. M2 receptor used was anti-mannose receptor (anti-MR), and the M2 cytokine marker was IL-10. The pan-macrophage marker used was anti-CD68. Using reverse transcriptase polymerase chain reaction, mRNA levels of M1 and M2 receptor markers and cytokine markers were quantified (N=1). The research is still ongoing.

RESULTS

The experiment is ongoing, but the preliminary results are as follows. Based on the AHA classification, the plaques were classified as Type V and Type VI. There are more M1 macrophages (based on anti-CD40 and TNF alpha) upstream > downstream > normal > central regions. There are more M2 macrophages (based on anti-MR and IL-10) upstream > downstream > normal > central regions.

CONCLUSIONS

There are different relative amounts of M1 and M2 macrophages in different regions of the human carotid plaques. The highest number of M1 and M2 macrophages is seen in the upstream region. The lowest M1 and M2 macrophage numbers are seen in the central lesion.
The Role of Breast Artery Calcification Detection in the Prevention and Detection of Coronary Artery Disease in Women

BACKGROUND

Coronary artery disease is the number one killer of women. Many women do not have "classic" symptoms and often ignore subtle warnings of this disease. Breast artery calcification (BAC) that is identified during screening mammography for breast cancer has been linked to coronary artery disease (CAD). If the link between BAC and CAD can be solidified, coupling the identification of breast artery calcification, as a potential marker for CAD, with existing breast cancer screening regimens could offer improved CAD detection in women and cost savings in disease screening.

OBJECTIVE

This study examined the relationship between BAC, as detected by mammography, and existing histories of heart disease, symptoms of CAD and risk factors for atherosclerotic heart disease in women presenting for breast cancer screening at an urban university hospital.

METHOD

This prospective cross-sectional pilot study of 140 English-speaking women evaluated data from a questionnaire administered prior to mammography screening. The questionnaire assessed for a history of coronary artery disease and risk factors for coronary heart disease. Mammograms were analyzed by staff radiologists blinded to the questionnaire responses. The data were analyzed to determine the relationship between the findings of BAC, a history of heart disease, symptoms of CAD, and presence of risk factors.

Findings: The incidence of BAC was 8.1% among the study population. The low number of BAC cases precluded multiple regression analysis. Chi-Square analysis revealed an association between dyspnea on exertion and BAC. There was a trend toward an association between angina or exertional chest discomfort and BAC. No cardiac risk factors were found to be associated with BAC.

CONCLUSIONS

Symptomatology for CAD differs between women and men. Women often have more subtle symptoms, such as shortness of breath and fatigue. The associations between shortness of breath and BAC, and exertional chest pain and BAC found in this research merit further investigation in a larger study. The design of the current study is appropriate for continued investigation.
Dabigatran toxicity in a 65 year old male who failed other anti-coagulation methods

When dabigatran was introduced to the US market in 2010 as an oral anticoagulant, it was heralded as a welcome alternative to warfarin. Among its reputed benefits, dabigatran does not require monitoring of levels. This case report describes a 65 year old male who developed dabigatran toxicity on the manufacturer’s recommended dosage. This patient likely developed dabigatran toxicity on the recommended dose due to concomitant amiodarone use. As a result of a number of post-marketing surveillance reports, the manufacturer recently changed the prescribing information to include warnings of interactions with PGP inhibitors, such as amiodarone. The recommended dose of dabigatran 150 mg twice a day may present added risk without dramatic added benefit over a lower dose for patients with atrial fibrillation. The FDA approved the higher dose because it wagered the added benefit of preventing systemic emboli outweighed the reduced risk of bleeding afforded by the lower dose. This case highlights that when prescribing dabigatran for a patient taking PGP inhibitors or inducers with concomitant chronic kidney disease, one should use alternate dosing and consider monitoring coagulation studies or drug levels.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Preliminary study evaluating the real time cerebral tissue oxygen index, as measured by near infrared spectroscopy, suggests that developmental delay seen in neonates undergoing complex repair for congenital heart defects is not solely due to transient decreases in brain oxygenation, but is likely a result of multifactorial variables.

BACKGROUND

An additional risk of brain injury followed by developmental delay has been documented for high-risk neonates with congenital heart defects (CHD) that undergo complex cardiac surgery. Despite improved techniques used during cardiothoracic surgery to minimize neural damage, little attention has been directed into the effects of decreased oxygen delivery and abnormal circulation in CHD. As a result, this study investigated the correlation between abnormalities in the real time cerebral tissue oxygen index (cTOI) as measured by near infrared spectroscopy (NIRS) during surgery and possible post-surgical neurologic deficiencies.

METHODS

NIRS was used intraoperatively to measure the real time cTOI for neonatal patients with hypoplastic left heart syndrome (HLHS) or transposition of the great arteries (TGA) who underwent the Norwood procedure or Arterial Switch, respectively. Follow-up evaluations of neurodevelopment were conducted through the Bayley Scales of Infant Development-II (BSID-II). Each neonate was assigned a total surgical bypass time, total time spent below 50%cTOI, and the rate of cTOI changes upon initiation of bypass. Additionally, the severity of oxygen depletion was assessed by measuring the extent and duration of deviation below 50%cTOI. These factors were compared to the neonates’ BSID-II scores at 6, 15, and 21 months. The R2 value for each correspondence was calculated to assess correlations between the above factors in regards to cTOI and the BSID-II scores. Based on previous literature, BSID-II scores below 70 were categorized as developmental delays, and cTOI below 50% was determined as a critical value representing cerebral hypoxia.

RESULTS

There were 26 HLHS and 13 TGA neonates who were monitored with NIRS. Correlations were calculated for the 15 HLHS and 12 TGA neonates with BSID-II evaluations. The BSID-II scores for HLHS neonates were as followed: mental (6m: 82.75, 12m: 82.55, 21m: 62); motor (6m: 68.25, 12m: 62.91, 21m: 62). The BSID-II average scores for TGA neonates were all above 70. R2 values suggested no significant direct correlation (HLHS: R2 all < 0.3210 and TGA R2<0.2400).

CONCLUSION

Neurodevelopmental delays seen in neonates who have undergone the Norwood procedure do not correlate isolated values of total bypass time, amount of time spent below 50%cTOI, rate of cTOI changes upon initiation of bypass, or severity of oxygen depletion. There were no developmental delays observed in TGA neonates. BSID-II scores post-Norwood procedures are likely a result of multifactorial components rather than the individualized factors.

Note: As this study is still in progress, the results reported are preliminary.
### SCHOOL OF MEDICINE AND HEALTH SCIENCES

**Prediction of Coronary Artery Disease via RNA Sequencing of Blood**

Cardiovascular diseases, particularly atherosclerosis, are the major cause of death and morbidity in developed countries. Atherosclerosis can lead to an acute myocardial infarction (MI), with an incidence of approximately 650,000 per year in the U.S. alone. The current gold standard for diagnosing coronary artery disease (CAD) is angiography via coronary artery catheterization. Surprisingly, despite some well-established clinical and diagnostic criteria, about 40% of the 1 million diagnostic catheterizations return a result of ‘no coronary blockage’. The goal of this project is to develop an assay performed on blood that will predict the presence of CAD in patients presenting with a clinical suspicion of heart disease, typically in the form of chest pain.

#### HYPOTHESIS

Patients who develop coronary artery disease produce specific changes in gene expression in whole blood RNA that are not present in patients without coronary artery disease.

#### METHODS

We employed innovative techniques to obtain high quality RNA from whole blood, combined with the most advanced next-generation sequencing (NGS) of RNA (RNAseq, aka ‘deep sequencing’) to recognize transcripts associated with CAD, or TRACs. Using this technique, we conducted a pilot study to identify TRACs in blood of up to 200 patients presenting for coronary catheterization. Blood RNA was depleted of ribosomal RNA and then RNA was sequenced on a Helicos Single Molecule Sequencer. The resulting short reads were aligned to the human transcriptome and the number of reads per kilobase of exon per million (RPKM) reads was determined.

#### RESULTS

From interim results on 20 patients, 10 with CAD vs 10 without CAD, we have established the ‘proof of principle’ that genome-wide transcript profiling can be accomplished, and that RNA transcripts exist which may have diagnostic value. More than 100 transcripts which differed more than 2-fold between groups with a p<.01 were identified. Examples include phospholipase D2 (PLD2), involved in cell signaling, and estrogen receptor-beta (ESR2) which has previously been identified as associated with CAD from genome-wide SNP analysis. Interestingly, serine hydroxymethyltransferase 2 (SHMT2) had one isoform elevated 4-fold, and another isoform reduced 4-fold, demonstrating the ability of RNAseq to detect changes in splicing during disease states.

#### CONCLUSIONS

If successful, these studies would provide a clinic-ready diagnostic test for the presence of CAD in chest pain patients. In the future, this test could be expanded toward diagnosing CAD in asymptomatic patients, which could potentially prevent unexpected MI and provide physicians the chance for early intervention.
Telecardiology Partnership between Washington, DC and Marrakech, Morocco: Supporting a Growing Pediatric Cardiovascular Service in the Developing World

BACKGROUND
Only 7% of the world’s population has access to modern pediatric cardiac surgery, resulting in nearly 6 million children with treatable conditions that are denied care. Telemedicine has the potential to help bridge this gap by providing remote consultation and distance education.

METHODS
Through grants from the Mosaic Foundation (Arab Ambassadors’ wives) and Intelsat, Children’s National Medical Center developed a telemedicine partnership with hospitals in Marrakech, Morocco. Our goal was to augment the skill level of the pediatric cardiovascular team through telemedicine and onsite visits. Videoconferencing units and satellite dishes were installed in 2009 with subsequent training in 2010. Our cardiovascular surgery team visited Marrakech in March 2010 and March 2011, performing 8 operations in 2011. We report on utilization, outcomes, barriers and sustainability of this program.

RESULTS
Live monthly videoconferences were started in 2009, increasing to weekly (Tuesdays-10 AM Washington/3 PM Morocco) in 2011 between the cardiovascular teams in Washington (CS, SS) and Marrakech (DB, YB). Patient data and echocardiograms were reviewed in real time. The Children’s technical team managed conferences remotely through our multipoint conference unit. 38 conferences occurred in the last 12 months. 14 were cancelled due to scheduling conflicts (none due to technical difficulties). 95 cases/73 patients were presented; 22 patients were discussed two or more times. Most common diagnoses were tetralogy of Fallot (n=14), transposition (n=10), double outlet right venticle (n=9), atrioventricular canal (n=8), and ventricular septal defect (n=6). Mean age was 4.8 years (3 days to 30 years). 44 patients were under age 2 years (average age 7 months). Mean oxygen saturation was 83%; 22 patients had a saturation of ≤ 80%. Additional imaging was recommended in 22 patients; considerable improvement in echocardiography skills was observed. Cardiac surgery was performed in 25% of patients discussed, more than half had a difference in approach as a result of the teleconference. Three operations (tetralogy of Fallot, atrioventricular canal, D-Transposition) were performed successfully in infants for the first time. Meetings with US and Moroccan government officials (including Ambassadors from both countries) have contributed to ongoing support. Focus on barriers including technology, satellite availability, language (most of the Moroccan team speaks English), funding and time difference has contributed to the success of the project.

CONCLUSIONS
Telemedicine is an innovative and practical means to augment the skills of pediatric cardiovascular surgery teams in the developing world. We are optimistic that our program will be sustainable for the foreseeable future.
GW MEDICAL FACULTY ASSOCIATES

Ultrasound evaluation of central venous catheter placement

Central venous access is critical for hemodynamic monitoring, delivery of blood products and drugs, total parenteral nutrition, management of perioperative fluids, and monitoring central venous pressure. However, mal-positioning of the central venous catheter (CVC) is common and can lead to morbidity and mortality. The catheter tip can be in the right atrium or right ventricle, which could lead to dysrhythmias, possible erosion through the cardiac chamber, or thrombus formation. Also, CVC tips can be in unintended blood vessels increasing the risk for infections or thrombosis or can puncture the lung, leading to a pneumothorax. The current practice for assessing proper placement of catheter tips is chest radiographs. Chest radiography requires time, manpower, and special equipments, which can hinder timely initiation of treatment for critically ill patients and expose patients to ionizing radiation.

This study is a prospective cohort study using bedside ultrasound to assess central CVC placement in Emergency Department, Operating Suites, and Intensive Care Units patients. We will obtain consent from patients that have met the inclusion criteria prior to central venous catheterization. At the conclusion of catheterization, during the step of flushing of the central catheter ports with sterile saline, the sonographer will time the routine injection of 10 mL of sterile saline with the transthoracic echocardiography and record the ultrasound examination.

We hypothesize that the echogenic signals from the saline flush, if immediately observed in the right atrium and/or ventricle, indicate the location of the catheter tip to be in the central venous circulation. We will compare the test characteristic of bedside ultrasound with post-CVC placement chest radiograph. If the test characteristics of bedside ultrasound are comparable or superior to the chest radiograph, this will present a potentially more efficient and cost-effective method to identify the accurate placement of CVC tips. In the future, this may obviate the ordering of chest radiographs in many patients whose accurate CVCs placement can be confirmed by ultrasound. Chest radiographs may continue to be performed for patients with inconclusive ultrasound findings, complicated procedures, or suspected mal-positioned catheter tip.
CARDOIOLOGY/CARDIOVASCULAR RESEARCH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Comparing Early and Late Angiography to Determine Progression of Graft Disease between the Radial Artery and Saphenous Vein Graft: Insights from the Radial Artery Patency Study (RAPS) – A Multi-Centered, Randomized Control Trial

Progression of graft disease can impair long-term graft patency after coronary artery bypass surgery (CABG). We compared the progression of disease between the Radial artery and Saphenous vein (SVG) over 5 years in patients who have undergone CABG.

561 patients <80 years of age undergoing primary isolated non-emergent CABG with 3-vessel disease and estimated ejection fraction >35% were enrolled across 13 centers. The left anterior descending coronary artery was bypassed using the left internal mammary artery. Within-patient randomization was performed for the study grafts; the Radial Artery was randomized to either the right or circumflex territory and the study SVG was used for the opposing region. Follow-up x-ray angiography was performed at year 1 and 5. The objectives were to determine the progression of graft disease in those that had TIMI 3 flow in both angiographies.

217 patients underwent both early and late angiographies. Mean early and late follow-up angiographies were 10±3 months and 7.5±1.3 years, respectively. Over 7 years, 94%(189/201) Radials vs. 92.6%(175/189) SVGs remained with TIMI 3 flow, p=0.58. Of these grafts, progression of disease from <30% stenosis to >30% did not differ between the Radial and SVG for the proximal and distal anastomosis sites. However, for graft body, 94.1%(174/185) Radials vs. 84.7%(144/170) SVGs, p=0.004, remained <30%, while 5.9%(11/185) Radials vs. 15.3%(26/170) SVGs, p=0.004, progressed to stenosis >30%.

Over 7 years, the SVG had significantly greater disease progression in the graft body compared to the radial artery. The radial artery may be superior to the SVG due to decreased graft body atherosclerosis resulting from differential graft biology.
DEPARTMENT OF HEALTH SCIENCES

Non-cardiac Fibroblasts and Cardiomyocyte Interactions to Develop a Cardiac Patch

BACKGROUND

It has been shown that in order to engineer cardiac tissue patches, one needs to combine both cardiac muscle cells and fibroblasts. In the past, only cardiac fibroblasts were used for this purpose. Our goal was to test whether or not non-cardiac fibroblasts, specifically NIH3T3 and WT-19 mouse fibroblasts, can substitute for cardiac fibroblasts to create functional cardiac patches. In addition, we also wanted to test a hypothesis that downregulation of Major Histocompatibility Complex Class I (MHC-I) molecules via inhibition of β2-microglobulin (β2-m) gene expression can minimize immunogenicity of these cells.

METHODS

WT-19 and 3T3 fibroblasts were grown on 5% and 10% FBS in DMEM respectively. 3D fiber structures were created by using Matrigel (Invitrogen) with varied concentrations of irradiated fibroblasts. Lethal irradiation was achieved by 13 minutes exposure to 60 Gy rays. Downregulation of MHC-I was achieved via transfection of WT-19 fibroblasts with anti-β2-m small hairpin RNA coding plasmid. Stably transfected cells were selected for 10 generations under G418 pressure.

RESULTS

The data demonstrated that different types of fibroblasts generate morphologically different 3D-fibers. When fibroblasts were irradiated to ensure optimal growth, so that they did not overgrow non-replicating cardiomyocytes, a well-structured bi-cellular network was formed. A proper ratio of fibroblasts to cardiomyocytes was needed to create optimal fibers. This was achieved with a 20:80 ratio, and a total amount of 2.5x10^5 cells per patch. The WT-19 fibroblasts created more robust fibers as compared to NIH 3T3 cells. We have also shown that downregulation of MHC-I molecules in WT-19 fibroblasts via inhibition of β2-microglobulin (β2-m) gene expression makes them less susceptible to T-cell recognition.

CONCLUSIONS

Non-cardiac fibroblasts can be used to create functional cardiac tissue patches. The proliferative capacity of these cells needs to be limited in order to prevent them from outgrowing non-dividing cardiomyocytes. Extracellular scaffold density has to be also adjusted to match with specific types of fibroblasts. Finally, downregulation of MHC-I decreases the immunogenicity of these cells.
INTRODUCTION

Ritonavir (RTV) and efavirenz (EFV) are first line anti-HIV agents, but their use may increase risk of co-morbid toxicity and cardiac dysfunction.

METHODS

We examined oxidative stress, lipid alterations and cardiotoxicity of RTV or EFV treatment (75 mg/kg/day by gavage) in Lewis-Brown Norwegian rats (160g) up to 8 weeks and assessed effects of dietary magnesium supplementation (Mg-Sup: 6-fold higher MgO). Cardiac functional and anatomical changes were monitored by in vivo echocardiography and histochemistry.

RESULTS

RTV enhanced plasma triglyceride (TG) levels early on (8 days) up to 8 weeks (40-80%; p<0.01) and increased cholesterol up to 5 weeks (35-40%; p<0.05). EFV only increased TG level (70%, p<0.01) on day 8. Mg-Sup completely (100%) suppressed RTV- or EFV-induced lipid abnormality. Blood neutrophils from RTV- and EFV-treated rats displayed 2.9-fold and 6.3-fold higher basal superoxide activity (p<0.01) and plasma 8-isoprostane levels rose 2.3- and 2.8-fold (p<0.05) at 5 weeks compared to vehicle controls. RBC GSSG/GSH ratios were increased 2.8- and 3.2-fold by RTV and EFV (p<0.025). RTV also decreased plasma nitrite level by 21% (p<0.025). Mg-Sup substantially (>75%, p<0.05) attenuated all these oxidative indices. At 5 weeks, both drugs caused significant decreases in shortening fraction (p<0.05) and mitral valve E/A ratio (p<0.05). At 8 wks, RTV caused a greater decline (14%) in shortening fraction versus EFV (10%). Both drugs decreased left ventricular posterior wall thickness in diastole (LVPWd: 8.5-10%) and systole (LVPWs:11-12%), indicative of progression toward dilated cardiomyopathy (p<0.05). Mg-Sup attenuated RTV-induced declines in systolic and diastolic function (>70%; p<0.05) and lessened LVPWs wall thinning (8 wks: by 75%, p<0.01). Partial protection (~ 50%) by Mg-Sup was observed in EFV-treated rats. Histochemical staining showed atrial WBC (CD 11b+) infiltration and ventricular fibrosis in 8 wk RTV and EFV hearts; both were diminished by Mg-Sup.

CONCLUSION

Prolonged use of RTV and EFV caused enhanced oxidative stress, hyperlipidemia, systolic and diastolic dysfunction and cardiac pathology. This study demonstrates the benefits of magnesium supplementation against HAART-induced cardiac toxicities. (Supported by NIH-R21NR012649)
Use of endogenous NADH fluorescence for real-time in situ visualization of epicardial radiofrequency ablation lesions and gaps

BACKGROUND
Radiofrequency ablation (RFA) is a commonly used treatment for atrial fibrillation and other arrhythmias. RFA works by eliminating abnormal sources of electrical activity and/or pathways for reentry by terminally damaging target tissue. One of the main shortcomings of RFA procedures is a lack of real-time visualization of the lesions. Our goal was to address this clinical need.

METHODS
We used blood-free and blood-perfused hearts from Sprague-dawley rats and New Zealand white rabbits in both ex-vivo and in-situ settings. RFA lesions were produced with a standard 4mm blazer RF catheter (EP Technologies, Boston Scientific Corporation). The lesions were created on the epicardial surface of the heart and imaged using a dual CCD-based fluorescence imaging system. The first channel employed UV-light illumination (360/50 nm excitation and 475/50 nm emission) to examine changes in endogenous NADH fluorescence. The second channel was optimized to image voltage-sensitive probe RH237 (530/35 nm emission and LP680 nm) and allowed us to monitor electrical activity near the lesions.

RESULTS
Significant change in epicardial NADH fluorescence was observed immediately after creating an RFA lesion. Staining with the vital dye TTC confirmed homogeneity and the extent of RFA lesions seen on fNADH channel. The interlesion profile of action potential amplitudes correlated with the interlesion profile of fNADH intensity suggesting that the latter can be used to evaluate the functional state of the tissue near the ablation site. Importantly, the feasibility of fNADH-based imaging in blood-perfused animals was also established. The latter was possible by displacing the blood between the epicardial surface and the camera lens.

CONCLUSIONS
By observing the endogenous fluorescence of NADH one can visualize location and degree of RFA injury in real-time. Applied to a clinical scenario, this information can reduce the time needed to accomplish RFA procedure where multiple lesions are required and minimize post-ablation recurrence of abnormal activity. This method can be implemented by adding a UV excitation/emission fiber-optic waveguide to the tip of RFA catheter.
Metabolic demand of fast rhythms in isolated working hearts and Langendorff perfused hearts

Accurate metabolic studies of the heart require that the heart perform work within the context of preload and afterload pressures, a feature unique to bi-ventricular (bi-V) working heart preparations. The objective of this study was to compare differences in the metabolic demand of fast rhythms in isolated bi-V working hearts and non-working Langendorff perfused hearts. Understanding such metabolic differences will aid in isolated heart studies of arrhythmias caused by ischemia and reperfusion. In this study, hearts from New Zealand white rabbits (n=8) were connected to a bi-V working heart system and perfused with modified Krebs-Henseleit solution at 37°C. Preload and afterload pressures were set at physiological values. An epicardial monophasic action potential electrode was used to monitor electrical activity while hearts were paced at cycle lengths (CL) of 300, 200, and 150ms. Fluorescence of NADH (fNADH) was imaged to monitor the redox state of epicardial tissue. To image fNADH, the epicardium was illuminated with filtered light (350±25nm) from a mercury lamp. Emitted light was filtered (460±20nm) and imaged using a CCD camera. Heart perfusion was then switched to non-working Langendorff mode and the pacing and imaging protocol was repeated. Changes in fNADH per unit time were measured and compared using N-way ANOVA tests. Statistical tests showed that fNADH increased during shorter CLs for both perfusion modes (p=0.001). Increases in fNADH per unit time were more than 5X higher at CL=150ms than other CLs (p<0.05). During bi-V perfusion, all increases in fNADH per unit time were higher than during Langendorff perfusion (p=0.007). Pacing rates closest to normal sinus rhythm resulted in minimal rise of fNADH for both perfusion modes. We have observed that fast rhythms elevate the redox state and, concomitantly, metabolic demand in both bi-V working and Langendorff heart preparations. However, elevations are much more rapid for working heart preparations, indicating that the time course of electrical alterations during acute ischemia and reperfusion could be very different between working and non-working heart studies.
Noninvasive monitoring and determination of arterial plaque burden by segmenting B-mode ultrasound images

BACKGROUND

The goal of this research is to establish a noninvasive, cost-efficient method for determining the degree of arterial narrowing in patients with arterial disease using only ultrasound images. Unlike current ultrasound methods for determining the degree of arterial stenosis, this method will use individual pixel characteristics to determine and define the plaque-intima boundary and plaque-lumen boundary to compute the plaque area and volume present within the imaged artery. Color flow duplex imaging is the current “gold standard” for noninvasive grading of arterial stenosis where grading arterial stenosis is based on the peak systolic velocity ratio. This, however, is not an exact determination of the degree of atherosclerotic plaque buildup, but rather is only an estimate of the degree of narrowing.

METHODS

Each image will be preprocessed before image analysis in the MATLAB environment to reduce noise and speckle inherent within the images. Each image will then undergo image segmentation, which is the partitioning of an image into pixel regions on the basis of pixel characteristics, to differentiate the plaque burden from the arterial wall and the blood. Segmenting the plaque burden from the surrounding tissue will allow area and volume determination to be carried out, providing a quantifiable measurement of the plaque burden within the diseased artery. We are currently working on obtaining access to patient ultrasound images of diseased and healthy carotid arteries.

RESULTS

From preliminary image analysis carried out on ultrasound images of the peripheral arteries it was determined that the process of image segmentation can successfully segment the plaque burden from the surrounding tissue. The segmentation results show the visual representation of the segmented plaque region. The area determination results provide a quantitative measurement of the plaque size. This area corresponds not to physical dimensions such as millimeters or centimeters, but the number of pixels included in the segmented region. Some quantitative data would be beneficial but given the preliminary nature of this work it is probably not possible to provide any numbers.

CONCLUSIONS

The proposed method may provide a more exact measurement of arterial plaque burden compared to color flow duplex imaging, and may also provide a noninvasive and cost efficient means to monitor and assess the effect that preventative medications, diet, and exercise have on plaque size.
In-vitro study of multi-scale secondary flows in a bent artery model under stent-induced perturbations

A kaleidoscope of vortical secondary flows appears in a curved artery model, at times with interesting secondary flow structures. These flows are represented by multiple streamwise vortex pairs under pulsatile flow conditions present in the human vasculature. In-vitro experiments are performed using phase-averaged particle image velocimetry (PIV). The vortices characterized by planar, counter-rotating pairs emerge through a 180 degree curved tube artery model subject to a physiological waveform measured by Holdsworth et al [1].

The motivation for this study stems from a variety of cardiovascular related phenomena that have secondary flow structures as a commonality. Atherosclerosis is generated in the curvatures of large arteries, wall shear stress in arteries, which is known to be closely related to atherogenesis and cellular biochemical response to mechanical factors such as shear stress on the endothelial cell lining the arterial wall.

A comparison of secondary flow morphologies at various locations in the bend were made for two scenarios viz.: flow with scaled model stent-induced perturbations and flow without the stent model (i.e. without perturbations). Stent-induced perturbations that may arise in arterial flows due to protrusions of implanted stents create transient unstable flow patterns. Strong secondary flows were observed during the deceleration phases of the physiological waveform. The phase-averaged flow fields of vorticity-, Q-criterion [2] -, Swirl number-, and continuous wavelet transform (CWT) indicate that the transitional flow patterns in the both perturbed and unperturbed flows. Dissipation of large scale vortices into multiple randomly located smaller structures is observed. While the breakdown into smaller vortices is primarily attributed to the stent-induced perturbations, the incidence of large scale structures arises from a combination of unsteady forcing and centrifugal instabilities. Transition to turbulence that is predominant during the deceleration phase, coupled with the multiplicity (number and scales) of coherent vortices led us to define the overarching goal of this research, i.e. characterization of secondary flow structure as a multi-scale problem. Our research is not only aimed at being clinically complimentary to but also informative about the richness of fundamental fluid dynamics associated with cardiovascular flows.

REFERENCES
Secondary flow vortical structures in curved arteries are known to alter the mechanical stimuli to the endothelial cells and affect the transport of platelets and monocytes to the vessel wall. Motivated by the associated fluid dynamics, an in-vitro investigation of secondary flows was performed using particle image velocimetry (PIV) in a bent-pipe model for curved arteries. Two-dimensional PIV flow field images were generated in a bent pipe model for curved arteries under physiological inflow conditions measured by Holdsworth et al [1]. Phase-locked, two-dimensional PIV images showed a multitude of coherent secondary flow structures of varying scales, counts and strengths. Unlike time-resolved measurements, phase-triggered measurements necessitate a large number of PIV images in an ensemble to fully understand the flow behavior. This poses an algorithmic challenge in vortical scale-count metrics since image-by-image analysis is prohibitively time consuming.

We introduce the concept of “Boundary tracing”, a method of identifying and isolating closed objects such as vortices in flow fields. This method that exhaustively post processes PIV image ensembles, incorporates coherent structure detection, automatic image thresholding (Otsu’ method [2]), pixel-isolation of coherent structures and circulation thresholding. The method has been successfully applied to in-vitro studies of blood flow in a curved artery model with and without perturbations induced by a model stent. Metrics of vortical scales, count and circulation were generated. A circulation threshold was established to enable resolution of finer scale vortical structures.

The potential of this method for studying blood flow is not restricted to PIV images but can be extended to magnetic resonance velocity imaging, both in normal subjects and in patients. The approach is promising, since it furthers our understanding of secondary flow behavior in curved arteries of the human vasculature.

REFERENCES
Effect of Dimethylarginine Dimethylaminohydrolase in the Development of Salt Sensitivity

BACKGROUND
High dietary salt intake has been associated with increased asymmetric dimethylarginine (ADMA), depressed nitric oxide metabolites (NOx), and greater vascular stiffness (AIx), particularly in salt sensitive individuals and African-Americans (AA). Thus, in normotensive AA, we explored whether dietary salt-induced depression in NOx was correlated with reduced dimethylarginine dimethylaminohydrolase (DDAH) (enzyme metabolizing ADMA), and if there were correlations between the magnitude of DDAH depression and increases in ADMA with changes in blood pressure (BP) and AIx.

METHODS
We conducted a 20-week cross-over study: 8-week low-sodium (100 mmol/day) dietary implementation (continued throughout the study) then randomization to 4-weeks 100 mmol sodium supplementation followed by 4-week wash-out period, then cross-over to placebo OR the exact opposite treatment sequence. Changes in urinary sodium:creatinine ratio, BP, AIx, urinary NOx, ADMA, and DDAH activity were defined as the difference between the end value of the respective treatment period (sodium - placebo).

RESULTS
The cohort included 43 normotensive African-Americans (female 87%) with mean age of 45 years. The mean level of DDAH activity and NOx were insignificantly lower post-sodium (DDAH: -0.83, p=0.39; NOx: -11.65, p=0.38); however, there was a positive correlation between the change in the NOx:creatinine ratio and DDAH activity (r=0.90; p<0.0001). The mean ADMA:creatinine ratio was insignificantly lower post-sodium (-0.164, p=0.52), and there was a significant positive correlation between the change in ADMA:creatinine and NOx:creatinine ratios (r=0.35; p=0.02), though a non-significant correlation between the change in ADMA:creatinine ratio and DDAH activity (r=0.19, p=0.21). Correlation of change between treatment periods in urine sodium:creatinine ratio with ADMA, DDAH, and urinary NOx:creatinine ratios were all non-significant (p=0.83, p=0.18, p=0.23, respectively).

BP levels post-sodium were insignificantly higher (SBP: +2.8 mmHg, p=0.27; DBP: +0.8 mmHg, p=0.66); while the difference in urine sodium:creatinine ratio was directly correlated to the difference in SBP and DBP (r=0.75, p=0.01; r=0.49; p=0.13, respectively). The between-treatment period change in ADMA:creatinine ratio was directly correlated to the change in SBP (r=0.37, p=0.07).

The AIx post-sodium trended higher by +11.79% (p=0.12). There were significant negative correlations of the change in AIx with changes in DDAH:creatinine and NOx:creatinine ratios (r=−0.61; p=0.04; r=−0.59; p=0.05, respectively).

CONCLUSIONS
The less than anticipated difference in urinary sodium:creatinine ratio between the treatment periods reduced study power, likely accounting for the insignificant trends in the main cross-over analysis. However, secondary analyses indeed confirmed the link between dietary sodium and depression of DDAH activity and NOx, as well as their measurable effects on vascular hemodynamics.
Validation of GeneExpert SA Nasal Complete Off Label Use for MRSA Inguinal Colonization in Cutaneous Abscess Patients

BACKGROUND
Methicillin resistant Staphylococcus aureus (MRSA) carriage is associated with risk of infection. Rapid MRSA screening if implemented in emergency departments (ED) could be an important infection control strategy. FDA-cleared GeneXpert® SA Nasal Complete assay (turn-around-time ~70 min) is approved for detecting S. aureus in nares specimens; real-time PCR targets include spa, mecA, and SCCmec genes. Objectives: 1) Validate GeneXpert® SA Nasal Complete assay for inguinal colonization 2) Determine proportion of ED subjects with cutaneous abscesses displaying nares and/or inguinal MRSA colonization and 3) Assess concordance between wound and colonization sites containing MRSA.

METHODS
Ongoing prospective study of adults 18 years or older in an urban ED presenting with abscesses who receive incision and drainage. Bilateral nares and inguinal swabs were obtained. Molecular testing was performed using GeneXpert® MRSA/SA SSTI assay for wound specimens and GeneXpert® SA Nasal Complete for nares and inguinal specimens. Culture was done by direct plating of swab on chrome agar, and if needed, TSB broth enrichment.

RESULTS
21 of 79 consented subjects were colonized with MRSA (21-inguinal and 15-nares). Subjects showed 84% concordance for MRSA in the wound with nares and 89% with inguinal, respectively. Compared to culture, pooled GeneXpert® demonstrated 83% sensitivity, 96% specificity, 91% positive predictive value, and 93% negative predictive value.

CONCLUSION
Off-label use of GeneXpert® SA Nasal Complete assay for inguinal colonization proved to be a rapid and accurate screening test. Interestingly, more people were colonized with MRSA in the inguinal region than nares; nares testing alone would have resulted in missing 29% of MRSA colonized subjects. In conclusion, inguinal as well as nares sites should be sampled when screening for MRSA colonization.
The Influence Of Ophthalmology Resident Surgical Simulator Training On Post-surgical Outcomes In Cataract Surgery

PURPOSE
To determine if ophthalmology surgical simulator use during ophthalmology residency training improves patient post-operative outcome in cataract surgery.

METHODS
29 residents were divided into simulator (N=13) and non-simulator (N=16) groups based on the use of the ophthalmology surgical simulator during their residency training. 158 cataract surgeries with residents as primary surgeons were retrospectively reviewed, 81 in the surgical simulator group, and 77 in the non-simulator group. Post-operative visual acuity, corneal edema, anterior chamber inflammation, and intraocular pressure were recorded. Each parameter was recorded on post-operative day 1, post-operative week 1, and post-operative month 1. Patients’ final best corrected visual acuity was also recorded. The visual acuity was calculated using the logMAR chart. Results of the two resident groups were compared using two-tailed T-tests.

RESULTS
Mean post-operative visual acuity was found to be 0.53 (20/68), 0.42 (20/53), and 0.19 (20/31) at post-operative day 1, post-operative week 1, and final best corrected visual acuity, respectively, for the simulator group. For the non-simulator group, the same findings were 0.62 (20/83), 0.52 (20/66), and 0.20 (20/32) respectively. In the simulator group, the mean post-operative corneal edema was 0.73, 0.33, and 0.04 at POD#1, POW#1, and POM#1 respectively. For the non-simulator group, the values were 0.74, 0.32, and 0.06. The mean post-operative anterior chamber inflammation was 1.56, 0.63, and 0.22 in the simulator group on POD#1, POW#1, and POM#1. For the non-simulator group, the values were 1.49, 0.73, and 0.25 respectively. The mean post-operative intraocular pressure on POD#1, POW#1, and POM#1 were 18.64, 15.11, and 14.11 respectively for the simulator group. The same values for the non-simulator group were 20.53, 13.96, and 15.11. Two-tailed T-tests did not reveal a significant difference between the two groups on all parameters (p>0.05).

CONCLUSIONS
Residents who trained using the ophthalmology surgical simulator had similar patient post-operative outcomes as residents who did not in the following parameters: best corrected visual acuity, corneal edema, anterior chamber inflammation, and intraocular pressure. This study provides evidence that use of a surgical simulator during residency training does not change patient post-operative course in cataract surgery.
The Influence of Race on Mortality and Morbidity Following Cardiac Surgery

OBJECTIVES

Current models of morbidity and mortality following cardiac surgery do not take into account all aspects of a patient’s pre-operative risk factors, including race. The objective is to determine if a patient’s race is an independent predictor of mortality and postoperative complications after undergoing cardiothoracic surgical procedures.

METHODS

Data from the Continuous Improvement in Cardiac Surgery Program (CICSP) Database were obtained. These data were prospectively collected on all patients undergoing cardiac surgical procedures at the Washington, DC Veteran’s Administration Hospital from November 1990 to February 2009. These data were analyzed to determine if race is a predictor of mortality, independent of other pre-existing risk factors (age, diabetes, smoking history, peripheral vascular disease, and creatinine level). These data were additionally analyzed to determine if race is also an independent risk factor for post-operative complications (perioperative myocardial infarction, acute renal failure, mediastinitis, return to the operating room for bleeding, prolonged mechanical ventilation, stroke, and coma).

RESULTS

Of the 2205 patients, 1599 were classified as Caucasian, 569 classified as African-American, and 37 were other (Native American, Hispanic, or other racial/ethnic groups). There was no significant difference in 180-day mortality between groups ($\chi^2=0.45$, p=0.50). However, deaths during the entire study period, show a significantly increased risk in the African-American group ($\chi^2=18.85$, p=0.00001). The Cox proportional hazards model also gives a significant hazard ratio=1.44 (95% CI: 1.08-1.91) for the African-American group.

Of the pre-operative risk factors evaluated, only PVD ($\chi^2=78.04$, p<0.00001) and diabetes ($\chi^2=16.52$, p=0.00005) were significant. This is corroborated by the Cox analysis, which showed a hazard ratio=1.47 (95% CI: 1.24-1.74) and 1.42 (95% CI: 1.20-1.69) respectively.

None of the post-operative morbidities, as listed above, showed significant $\chi^2$ values, for either the Caucasian or African-American groups.

CONCLUSIONS

Immediately following cardiac surgery, race is not a significant influence on mortality or post-operative complications. However, over time, there is a significant risk to survival for those in the African-American group. The presence of peripheral vascular disease and diabetes are additional risk factors, and careful consideration to a history of these should be given when planning cardiac surgery for these patients.
SVC Enhances Flow Spirometry’s Detection of Obstruction

BACKGROUND
Flow spirometry is performed to determine whether dyspnea is due to airflow obstruction. Airflow obstruction is defined by FEV1/VC < 70%. In many clinical settings, forced vital capacity (FVC) is the only spirometric measurement of vital capacity (VC). Slow vital capacity (SVC) may be larger than FVC. We’ve reviewed our spirometry data to determine whether concomitant measurement of SVC with flow spirometry, and calculation of FEV1/VC using the largest VC, improves sensitivity of the test for diagnosis of airflow obstruction.

METHODS
We reviewed spirometric measurements of 3305 consecutive patients who had flow and SVC measurements. Tests were performed at the Washington VAMC Pulmonary Function Laboratory 2001-5. Tests were excluded if measurements did not meet ATS/ERS performance standards. Using community standard prices, we estimated the cost of additional testing which could have accrued in patients with dyspnea whose obstruction was missed without SVC measurement.

RESULTS
50% of the 3305 patients had normal spirometry, defined by FEV1/FVC ≥ 70%. 581 of the total 3305 (17.6%) had SVC > FVC by greater than 200 ml. 216 of the 581 had normal FEV1/FVC. In 116 of these 216 (54%), airflow obstruction was identified when FEV1/VC was calculated with the larger SVC. Estimated annual savings in our population was $55,000 USD.

CONCLUSIONS
Adding measurement of slow vital capacity to the standard forced spirometric measurements may improve the sensitivity of spirometry for detecting airflow obstruction, and save money in the management of patients with chronic dyspnea.
BACKGROUND:
The authors present an unusual case of bilateral medial foot compartment syndrome in a healthy female after Zumba, a low-intensity dance aerobics class. Compartment syndrome is an increase in pressure in an anatomic compartment that leads to soft tissue damage. The majority of compartment syndrome cases have occurred after trauma, such as combat crush injuries and motor vehicle accidents. There are a paucity of cases on the clinical management and follow-up of this rare occurrence of compartment syndrome.

CASE PRESENTATION
A 21 year-old healthy woman attended a fitness class and subsequently experienced significant pain in both arches of her feet. The emergency department discharged her twice with pain medications. She was found to have increased compartment pressures in both feet after a podiatry work-up. The patient underwent bilateral fasciotomies in the operating room and gained full recovery after eight months.

DISCUSSION
Previous compartment syndromes of the foot were primarily the result of discrete trauma. This is an unusual presentation of foot compartment syndrome in a recreational athlete after a Zumba class. Untreated compartment syndrome can lead to debilitating consequences, (plantar contracture, nerve paresthesias, and limb deformity). The clinical picture of compartment syndrome requires astute clinical suspicion complemented by diagnostic measurements and surgical treatments.

CONCLUSION
This unique case report is of interest because of the patient’s low-risk demographical characteristics, anatomic location, and bilateralism. Clinicians in many fields may come across cases of foot compartment syndrome and should understand the urgency of this clinical scenario.
Case Report: A Jane Doe with a very low calcium level

**OBJECTIVE**
To discuss the clinical and radiologic findings of a rare presentation of altered mental status in an adult.

**METHODS**
Case report and literature review.

**CASE PRESENTATION**
A middle-aged African American woman of unknown identity presented to the emergency department with altered mental status and facial trauma. Initial evaluation revealed a serum calcium of 6.1mg/dL (reference range 8.6-11.0 mg/dL) and an unenhanced CT scan of the head with extensive calcification involving the deep aspects of the cerebellar hemispheres, basal ganglia, thalami, and subcortical supratentorial white matter bilaterally. These findings, along with a significantly elevated parathyroid hormone level of 972 pg/ml, were consistent with a diagnosis of pseudohypoparathyroidism (PHP).

**DISCUSSION**
PHP consists of a group of heterogeneous disorders with a genetic component and is typically present in childhood. Subtypes of PHP often exhibit characteristic features such as round facies, short stature, short fourth metacarpal bones, and developmental delay. We present a case of a patient exhibiting normal physical features with no significant family history, consistent with a diagnosis of PHP type 2. Symmetrical intracranial calcifications are associated with longstanding abnormal calcium and phosphate metabolism, such as occurs in pseudohypoparathyroidism, however the underlying mechanisms remains unclear. Patients with such extensive cerebral calcifications can develop a range of neurological symptoms, such as mental status changes that our patient displayed. This case displays a rare presentation of altered mental status in an adult as opposed to being diagnosed at a younger age.
African Americans may have more colonic adenomas at the time of initial screening colonoscopy

**PURPOSE**

African Americans have more morbidity and mortality from colon cancer than other ethnic groups in the United States. Adenomatous polyps are a major risk factor for the development of colon cancer. There is limited data evaluating the presence of adenomatous polyps at the time of initial screening colonoscopy based upon patient race. This study assessed the number of colonic adenomas at the time of initial screening colonoscopy in a university gastroenterology practice.

**METHODS**

The medical records of patients referred for a colonoscopy to a university gastroenterology practice during a 6-month period were evaluated. Patient age, gender, and race were obtained. Patients were included if they were at average risk for the development of colon cancer and were referred for their initial screening procedure. There were no exclusion criteria. A database, maintaining patient confidentiality, was created. Statistical analysis was performed using a Fisher Exact test with significance set at p<0.05.

**RESULTS**

600 patients were referred for a screening colonoscopy and 344 (217 women, 127 men) had the procedure. 196 of the 344 patients (57%) were African American (AA) and 148 (43%) were of another race. 86 (14.3%) had adenomatous polyps with an average polyp number of 1.63. In the 196 AA patients (126 female, 70 male), 54 (27.6%) had polyps with an average polyp number of 1.79. 30 AA women had polyps with an average polyp number of 1.89. 24 AA men had polyps with an average polyp number of 1.67. In the 148 non-AA patients (91 female, 57 male), 29 (19.6%) had polyps with an average polyp number of 1.34. 20 non-AA women had polyps with an average polyp number of 1.25. 9 non-AA men had polyps with an average polyp number of 1.56. While AA patients had a greater number of polyps compared to others, the rate approached, but did not meet statistical significance. (p=0.06). AA females had significantly more polyps compared to non-AA females (p=0.027). There was no significant difference (p=0.818) in the number of polyps in AA men and non-AA men.

**CONCLUSION**

Colon cancer causes significantly morbidity and mortality in African Americans. Adenomatous polyps are a significant risk factor for the development of colon cancer. There have been limited studies, which have evaluated the presence of colonic adenomas at the time of initial screening colonoscopy. This study revealed that AA women had significantly more adenomatous polyps at the time of initial screening colonoscopy when compared to other women. Further investigation with a larger cohort of patients will allow for greater understanding of the potential role of patient race and the prevalence of adenomas during screening colonoscopy.
A commonly occurring injury afflicting the pediatric population is the fingertip injury, which may range from a simple superficial laceration to a complete amputation. This study aims to determine the epidemiology, treatment algorithm and follow-up, and cost of fingertip injuries in the pediatric population presenting at Children’s Hospital Boston.

Methods
Data was collected over a five-year period (January 2005 to January 2010) from Children’s Hospital Boston of pediatric patients under the age of 21 at time of injury, identified by ICD9 code 883.0-.3, representing fingertip injury. Data collected included gender, age, date of birth, date of injury, hand and finger injured, mechanism of injury, nailbed versus non-nailbed, presence of fracture, presence of amputation, emergency room and operating room treatment, number of follow-up appointments, and cost.

Results
Data is still being collected for this study.

Conclusion
The analysis of the epidemiology of fingertip injuries in the pediatric population could provide the community with great information regarding hospital treatment course and follow-up, along with cost-effectiveness, for these patients.
Utilizing Smartphone Applications to Monitor Diabetes

BACKGROUND
Mobile phone technology is now being applied to chronic disease management through the use of real-time physiologic monitoring, two-way communication, data transmission between patient and provider, and real-time data analysis and decision support. There have been several trials of mobile health ("mHealth") technologies in chronic conditions including HIV/AIDS, asthma, hypertension, obesity, and smoking cessation. People with diabetes are likely to benefit from the capabilities of cell phones in health care because effective diabetes care requires ongoing, active management by a well-informed patient. Numerous cell phone apps for diabetes care are now available. These apps perform functions including logging blood sugar and diet records, monitoring physical activity, providing access to diabetes education materials and providing motivational support to patients. However, to date there have been no comprehensive surveys of the features and potential strengths and weaknesses of currently available apps. The purpose of this study was to perform such an analysis in order to assist patients and doctors in choosing from hundreds of applications based on standardized criteria.

METHODS
Criteria to evaluate diabetes management applications were developed. These criteria included whether or not the application had a function to log and track physiologic data such as blood glucose levels, weight, etc., whether the application provided diabetes education, whether the application enabled patient networking and whether the application provided diabetes management recommendations. We also evaluated whether or not the application had a commercial tie, if it was oriented towards intensive insulin therapy, if there was a specific target group, if there were help functions and whether or not it followed American Diabetes Association (ADA) guidelines and/or American Association of Diabetes Educator (AADE) guidelines.

RESULTS
299 Apple iPhone applications, 211 Google Android applications and 43 Blackberry applications were selected by searching the following key words: “Diabetes,” “Insulin,” and “Glucose.” These apps are being evaluated on the above criteria, and this analysis is currently underway.

CONCLUSIONS
As of today, no conclusions can be made.
**SCHOOL OF MEDICINE AND HEALTH SCIENCES**

**Evaluation of Anesthesia Residency Department Program Directors and Web Sites establishes preliminary insights and aims of Anesthesia Residency programs**

**BACKGROUND**

Web site content and design features for Anesthesiology departments’ vary greatly. Variance may reflect the incorrect assumption that Web sites are primarily targeting medical students applying to residency programs. Therefore, the purpose of this study was to further establish primary and secondary audiences for these sites, to investigate their design and maintenance, and to determine residency program directors involvement in department Web sites.

**METHODS**

An anonymous web-based survey for anesthesiology program directors was conducted through the Academic Anesthesiology Core Program Directors (AACPD) listserv. Ten questions consisting of 35 items sought to determine program director(s): demographic information, level of involvement, comfort level, familiarity with other Web sites, as well as frequency of Web site updates, cost allocated to Web site management, and targeted audiences for anesthesiology department Web sites. Additionally, all Accreditation Council for Graduate Medical Education (ACGME) anesthesiology department Web sites were independently evaluated for 60 items grouped into 11 categories and assessed based on a binary system (Yes/No).

**RESULTS**

The survey was completed by 42 of 131 (32%) program directors. It was determined that program primarily directed information to a Webmaster in the anesthesiology department (n=17, 40.5%). Web sites were most commonly updated annually (n=20, 47.6%). Top 3 targeted audiences: medical student applicants, medical students at the host institution and current residents. 85% felt that a Web site is ‘very’ important in the recruitment of medical student applicants. 33% felt their department Web site is a ‘very’ important tool for communication with other audiences (faculty and staff, alumni, donors, and or patients). The majority of program directors ‘sometimes’ or ‘often’ looked at Web sites to determine trends in content (95%), while less experienced program directors (<2 years) were more likely to look ‘often’ at other departments’ compared to program directors(<3 years).

**CONCLUSION**

Though program directors reported medical student applicants to be the primary audience targeted by the department’s Web site, information typically intended for applicants was only found on 42% of all Web sites. Prior studies indicate that residents access to personal schedules, including block and call, and program event information as the greatest information needs, but was typically absent from the public department Web sites. The majority of programs reported updating their Web site annually, likely tailored to applicants applying to residency programs each year or due to limited resources, where program resources ranged from $0 to $7000.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

An evidence based algorithm for the use of neuroimaging in the setting of a mass casualty event for the evaluation of traumatic brain injury

OBJECTIVE

Mass casualty events have the ability to cause disruption to even the most sophisticated hospital system. The injuries incurred by victims are as diverse as the events themselves and may impact any system in the body. As of yet, there exist no clear guidelines to triage patients suspected of traumatic brain injury as to which patients should receive a cranial CT-scan.

METHODS

A review of the literature was performed using the terms Traumatic Brain Injury, Imaging, Disaster and Mass Casualty Event with the search engines Medline and PubMed.

RESULTS TO DATE

It is clear that there are numerous signs and symptoms, which in the setting of cranial trauma, would suggest a patient should receive a cranial CT-scan. However, there is great variance between the specificity and sensitivity of these symptoms for detecting intracranial pathology. Age over 65, headache and posttraumatic amnesia have much lower odds ratios than the other criteria. Furthermore, criteria such as a dangerous mechanism of injury would not be specific in a mass casualty event or disaster.

CONCLUSIONS

By eliminating criteria with lower predictive value for intracranial pathology, it is possible to create a more streamlined decision tree as to which patients would require a cranial CT-scan in the setting of a mass casualty event. Symptoms such as vomiting, neurologic deficit or signs of basilar skull fracture present in a patient would still require cranial imaging.
Balloon dilation with corticosteroid injections: a durable endoscopic option for Crohn’s-related pyloric stenosis

INTRODUCTION

Pyloric stenosis due to Crohn’s disease is relatively rare. There is no consensus regarding the management of this complication. Fibrostenotic lesions in Crohn’s disease are typically resistant to pharmacologic therapy. Patients with gastroduodenal Crohn’s disease often require surgical intervention. Balloon dilation with or without corticosteroid injections have been found to be effective in the management of stenosis in the distal small bowel and colon. We report a case which illustrates that intralesional corticosteroid injection and balloon dilation of Crohn’s-related pyloric stenosis is an effective and durable intervention.

CASE

A 25 year old Caucasian woman presented with a 1 year history of progressive nausea, vomiting, bloating, abdominal pain and intermittent diarrhea. An upper endoscopy showed pyloric stenosis with biopsies revealing chronic active inflammation and non-caseating granulomas. There was no evidence of Helicobacter pylori. A subsequent colonoscopy revealed scattered areas of erythema interspersed with normal mucosa in the terminal ileum and colon. Biopsies revealed chronic active inflammation with non-caseating granulomas. She was treated with mesalamine and 6-mercaptopurine with improvement of her abdominal discomfort and resolution of her diarrhea. However, she had persistent nausea, vomiting, abdominal distension and unintentional weight loss.

Controlled Radial Expansion (CRE) balloon dilation to 8 mm was performed of her pyloric stenosis with some improvement of her symptoms. During the subsequent 18 month period, she underwent 5 endoscopies with triamcinalone injection and CRE balloon dilatation (to maximum of 15 mm) of the pylorus with progressive improvement and ultimate resolution of her symptoms. She has been maintained on mesalamine and 6-mercaptopurine for 10 years with no recurrence of her obstructive symptoms.

DISCUSSION

Crohn’s disease is frequently complicated by fibrostenosis. Pharmacologic management often is attempted, however ~30% of patients will require surgical intervention. Post-operative course is often complicated by recurrence. Avoidance of surgical intervention is desired if possible. Endoscopic management of fibrostenosis may alleviate the need for surgical intervention in selected patients. This case demonstrates a durable endoscopic approach to the management of pyloric stenosis due to Crohn’s disease.
Prevertebral Calcific Tendinitis of the Longus Colli - A Case Report

OBJECTIVES
To recognize that prevertebral calcific tendinitis of the longus colli is a rare inflammatory non-infectious cause of retropharyngeal fluid. To understand that appropriate treatment of this condition is with anti-inflammatory medications rather than antibiotics and/or surgical drainage.

METHODS
We report a rare case of retropharyngeal effusion caused by prevertebral calcific tendinitis of the longus colli muscle. A Medline query for prevertebral calcific tendinitis, retropharyngeal calcific tendinitis, hydroxyapatite deposition disease of the neck was performed for literature review.

RESULTS
Prevertebral calcific tendinitis of the longus colli is a rare entity that may cause an effusion which could be misdiagnosed as a retropharyngeal abscess. Our patient presented with a three day history of worsening neck pain and stiffness, and dysphagia. There was no fever and, he had a normal white cell count. Contrast CT scan revealed a non rim-enhancing, non-bulging retropharyngeal fluid collection and calcification of the longus colli tendons near the C2 vertebrae. One dose of intravenous dexamethasone was administered and the patient's neck stiffness markedly improved. A steroid taper was prescribed and his symptoms had completely resolved at two-week follow-up.

CONCLUSION
Prevertebral calcific tendinitis of the longus colli may cause a retropharyngeal effusion mimicking abscess. Prompt diagnosis can be made by recognizing the characteristic CT findings in the context of absent clinical evidence for infection. Anti-inflammatory medications are the treatment of choice.
Biofeedback in the treatment of chronic back pain [Review]

Chronic back pain is a common complaint among U.S. citizens. There are many traditional therapeutic approaches to treat this pain, which include medications and surgery. Unfortunately, these traditional approaches do not work for all patients. Biofeedback is an alternative medical treatment for chronic back pain that has been shown to be efficacious enough to either complement or, in some cases, replace traditional methods. Biofeedback is the process of using different techniques to teach patients how to control their physical movements in order to improve their health and physical performance. Electromyography (EMG), which records the electrical activity of muscle, is typically used to help patients learn to make movements that cause more or less stimulation of different muscle groups. The goal is to have patients modify their movements and muscle group usage in order to control their chronic back pain. Many studies have been done in recent years but reported efficacy varies widely. This variation appears to be at least partly related to a lack of standardization in patient selection, as well as differences in measuring outcomes. This poster will showcase the studies that have shown the most efficacy, and will highlight how and when biofeedback can be a stand-alone treatment or a complement to traditional treatment modalities.
Polymorphisms Associated with Physical Activity and Body Composition

OBJECTIVE
To explore whether six single nucleotide polymorphisms (SNPs) previously demonstrated to be associated with adult leisure-time exercise behavior in an older population (mean 45.9 years) – rs12405556 in the LEPR gene, rs10946904 in the PRSS16 gene, rs1766581 in the SIPA1L2 gene, rs2762527 in the PAPSS2 gene, rs9633417 in the SGIP1 gene, and rs6679293 in the DNASE2 gene – are associated with body composition, strength, change in strength after an intervention (resistance training), and measures of physical activity in two healthy, college-aged populations of men and women.

SUBJECTS AND METHODS
We genotyped six SNPs in two healthy populations. First we studied individuals enrolled in a resistance-training program of the non-dominant arm (n = 753 volunteers, mean 24 years), from the FAMUSS cohort. We measured associations of the SNPs with these phenotypes: whole arm muscle (MRI), subcutaneous arm fat (MRI), bone volumes of the arm (MRI), 1-repetition max (1RM) and elbow flexion strength, before and after 12 weeks of resistance training.

Second, we examined the influence of the SNPs on physical activity levels and body measurements in 136 healthy subjects (67 males and 69 females, mean 22.5 years), from the MB-UMASS cohort. In this study, subjects completed the International Physical Activity Questionnaire, and were measured for four criteria (by DEXA): bone mineral density, lean mass, fat mass, and percent tissue fat.

Hardy-Weinberg equilibrium was validated for each SNP. Associations between SNPs and phenotypes were tested using ANCOVA. For those with a significant F-test, pair-wise comparisons were performed and p-values adjusted for multiple comparisons using the Sidak method. Each model included appropriate covariates.

RESULTS
We found two SNPs to be associated with strength/muscle measurements in the FAMUSS population: rs10946904 with baseline and change in 1RM in men, and rs12405556 with change in muscle volume in women. We found three SNPs to be associated with body measurements: rs12405556 with baseline total bone volume, total fat, and total lean mass, all in men; rs10946904 with baseline subcutaneous fat in women; and rs1766581 with bone mineral content in women. Finally, we found two SNPs to be associated with total physical activity – rs10946904 with male activity and rs2762527 with female activity.

DISCUSSION
We found that numerous variants, previously associated with physical activity in an older population, effect body composition in young individuals. In a separate population, we found associations with muscle strength and response to resistance training. The same genotypes that were associated with response to training were associated with physical activity. These variants may influence skeletal muscle response to resistance training and may respond to aerobic intervention. This needs further exploration in different populations. Finally, being able to corroborate previous findings for two SNPs regarding their association with leisure-time exercise further supports their significance.
Ultrasound Guided Needle Localization of Parotid Stones during Open Sialolithotomy

Background
The current treatment modality in the United States for parotid sialolithiasis is either partial or total parotidectomy. With either method, loss of glandular tissue and subsequent function is a common complication. Alternative modalities exist in international literature and include therapies such as acoustic shockwave lithotripsy and transcutaneous approaches with endoscopically assisted localization. In the United States, acoustic shockwave lithotripsy is limited by lack of FDA approval and because parotid sialolithiasis has proven to be refractory in greater than 10% of cases internationally. Minimally invasive transcutaneous approaches after endoscopic assisted localization for stone removal are thought to be successful. However, only a few international sources in the literature support its efficacy to date. Thus, alternative less invasive methods need to be investigated. Ultrasound guided needle localization of parotid stones during open sialolithotomy offers an additional modality as treatment for parotid sialolithiasis.

Methods
Five patients were included in the study. All patients who were treated at the George Washington University and underwent US guided needle localization of parotid stones during open sialolithotomy were identified. This report retrospectively examines the 5 cases.

Results
5/5 subjects were subject to post-operation follow-up. All 5/5 (100%) cases were successful without complications or refractory stones.

Conclusions
Ultrasound guided needle localization of parotid stones during open sialolithotomy should be considered as a minimally invasive modality to treat primary and refractory cases of parotid sialolithiasis in the United States and international populations.
Clinical Specialties

School of Medicine and Health Sciences

Cleft Care in International Adoption

Purpose

Standards of cleft care abroad often differ considerably from what is expected in the United States, especially in less developed countries where international adoption rates are high. Children with cleft lip/palate deformities adopted from these countries present to plastic surgeons in the United States in various states of repair and often at ages well beyond accepted treatment norms. The operative and perioperative needs of these children necessitating surgical intervention upon arrival in the United States are poorly understood. This is the first study to characterize the pre-adoption history, the post-adoption course, and surgical outcomes of adopted children with cleft lip/cleft palate deformities.

Methods

We performed a long-term retrospective review of all adopted cleft lip/palate patients presenting to an academic craniofacial referral center. Pre-adoption medical records (when available), craniofacial clinic charts/ACPA database, and operative reports were analyzed for demographic characteristics, pre-adoption history, post-adoption interventions, and outcomes.

Results

Between May, 1993 and August, 2010, 83 adopted children with cleft lip/cleft palate deformities were evaluated in our craniofacial center. Average age at adoption was 30.5 months (range 5.0-95.0 months). Originating countries were predominantly China (78.4%), Russia (12.1%), and Ukraine (4.8%). Table 1 describes the diagnoses of our patient population. Pre-adoption medical records were available for 21.8 percent of patients. 76.4 (n=42) percent unilateral cleft lip patients and 73.9 (n=17) percent of bilateral cleft lip patients were repaired prior to adoption at an average age of 10.8 months (range 5.4-15.5 months). 32.8 (n=22) percent of patients with cleft palate deformities were repaired prior to adoption at an average age of 25.6 months (range 8.4-40.0 months). Table 2 describes the post-adoption procedures performed on our patient population. Average age of post-adoption primary repair was 17.8 months (range 7.6-23.7 months) for unilateral cleft lip deformities, 21.5 (range 8.4-40.0 months) for bilateral cleft lip deformities, and 27.9 months (range 10.5-85.9 months) for cleft palate deformities. There were 6 (27.27%) clinically significant fistulas in patients who underwent pre-adoption palate repair compared to 8 (22.22%) in patients who underwent palate repair post-adoption (p=0.45). Hypernasal speech developed in 9 (40.91%) patients who underwent pre-adoption palate repair compared to 22 (61.11%) patients who underwent palate repair post-adoption (p=0.11), while velopharyngeal insufficiency was observed in 3 (13.64%) patients who underwent pre-adoption palate repair compared to 7 (19.44%) patients who underwent palate repair post-adoption (p=0.43). When assessing the quality of the lip repairs, 28 (47.46%) patients who underwent pre-adoption lip repair compared to 7 (41.18%) patients who underwent lip repair post-adoption (p=0.43).

Conclusion

The adopted cleft patient represents a complex and variable population with high rates of revision and delayed presentation. Surgical outcomes are poor in these patients compared to non-adopted populations.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Change in Sagittal Balance with Interlaminar Decompression and Spinal Process Fusion (ILIF)

INTRODUCTION

The Interlaminar Lumbar Instrumented Fusion (ILIF) device is an effective agent in relieving lumbar stenosis and spondylosis. It blocks extension at the affected level relieving neurogenic claudication. This device and similar ones have been criticized for producing local kyphosis, which in turn could contribute to sagittal imbalance. Sagittal imbalance is known to be a major predictor of a poor quality of life. Yet there is no previous data on the effect of the ILIF on overall sagittal balance.

METHODS

A prospective study with 15 patients undergoing ILIF procedure was initiated. Their spines were x-rayed preoperatively and postoperatively with 36-inch standing anteroposterior and lateral radiographs. Preoperative and postoperative sagittal balance was measured with a C7 body plumb line on both films and the difference was measured (positive versus negative standardized). The lumbar and instrumented level Cobb angles were compared pre and postoperatively using the same radiographs.

RESULTS

Full-length spine radiographs showed minimal change in sagittal balance after ILIF procedure. The average change was a 0.24cm improvement in sagittal balance, with a range from a 5.55cm of increased global lordosis to -5.42cm of worsening and kyphotic posture. On average, lumbar lordosis increased 0.34 degrees, while the instrumented Cobb angle decreased by 2.54 degrees.

DISCUSSION

This study does not demonstrate a significant alteration in sagittal balance after ILIF implantation. In fact, the data shows a small improvement in sagittal balance. Because kyphogenic implants minimally alter biomechanics at adjacent levels, the remaining spine can appropriately compensate. With a local kyphogenic implant in place, foraminal height and width, as well as disc height, increase. The affected level will no longer be stenotic, and the patient can assume a more upright posture with less radicular symptoms. This could lead to better quality of life in addition to relief of radiating neurologic symptoms.

CONCLUSION

Previous studies of interspinous process fusion and spacers have examined segmental lordosis, disc angles, and other parameters. This study is the first to examine overall spinal balance on full-length films after ILIF procedure. ILIF and similar devices minimally alter the sagittal balance, and in many instances improve it.
Difficult Airway in a Patient with Cornelia De Lange Syndrome

The patient with Cornelia de Lange can present many challenges to an anesthesiologist. The patient in our case report had many of the stigmata of the syndrome including dysmorphic facial features (micrognathia and characteristic arched and joined eyebrows), severe developmental delay, cardiac abnormalities (tetralogy of Fallot) and skeletal abnormalities. Consequently, the patient also had an extensive medical and surgical history including a repair of tetralogy of Fallot and a tracheostomy secondary to respiratory failure associated with recurrent aspiration pneumonias. By history, the patient was difficult to intubate and limited airway exam indicated a potentially difficult intubation.

The difficult airway algorithm exists to aid the anesthesiologist in the approach to the patient with a potentially challenging airway. Given the history and physical exam, the difficult airway cart was immediately available for the anesthesia team.

The patient in this case presented additional challenges because of her severe developmental delay and inability to cooperate with care. In addition, any sedative/hypnotics needed to be administered with caution given an incomplete cardiac history and loss to followup. After premedication with midazolam, the patient was taken to the interventional radiology suite and an IV was placed. A slow IV induction, provided for a smooth transition allowing the anesthesia team to establish control of her airway with manual mask ventilation. Once the ability to mask ventilate had been established, the depth of anesthetic could be titrated to allow for placement of a definitive airway using a nasal fiberoptic approach. Prior tracheostomy resulted in subglottic scarring, limiting the size of the endotracheal tube that could be inserted into the trachea.
OBJECTIVES/BACKGROUND
Two coding variants in the apolipoprotein L1 gene (APOL1) are strongly associated with the development of focal segmental glomerular sclerosis (FSGS) in African Americans in an autosomal recessive pattern of inheritance. However, the clinical significance of these two genetic variants in patients with biopsy-proven FSGS is still poorly understood. We sought to evaluate whether APOL1 genotype affects chance of progression to end-stage renal disease (ESRD), time to ESRD, recurrence or FSGS or graft failure if patients required kidney transplant, creatinine if there was no progression to ESRD, and response (complete or partial) to immunosuppressants used in the treatment of FSGS.

METHODS
In this retrospective cohort study, we collected data from medical records of patients diagnosed with FSGS by kidney biopsy and treated at the Glomerular Center of the Columbia University Medical Center (n=51). Medical records with sufficient information to indicate clinical progression and response to treatment were available for 30 patients. APOL1 genotyping for each patient was performed at the Laboratory of Inherited Kidney Disease at Beth Israel Deaconess Medical Center and Harvard Medical School. Due to a limited sample size, the data has not yet been statistically analyzed.

RESULTS TO DATE
Results are not yet available. Additional medical records must be located in order to increase the sample size so that the results of statistical analysis will be significant.

CONCLUSIONS
Pending data analysis.
Neuropsychiatric manifestations of SLE (NPSLE) is an elusive clinical diagnosis that can present in a variety of ways, from neuropathy to psychosis. Similarly, the psychiatric sequelae of trauma are seemingly unique to individual patients, and can include depression, paranoia, or florid psychosis. This case describes a 21-year-old African American female with a history of periorbital edema and long-standing trauma who presented to the ED with acute agitation and paranoia. During her stay on both psychiatric and medicine floors, JL demonstrated auditory hallucinations and paranoid ideation. Her physical exam was remarkable for periorbital and facial edema; initial laboratory results were remarkable for anemia, and eventual rheumatologic workup revealed +ANA, + anti-smith and anti-dsDNA antibodies, elevated CSF protein, and an abnormal PET scan. Treatment with oral prednisone resulted in diminished paranoia, denial of auditory hallucinations, resolution of facial edema, and upward trending hemoglobin and hematocrit.

This case demonstrates the ability of a cerebral vasculitis to masquerade as an emerging psychiatric disorder. Up to 8% of patients with SLE experience psychosis as part of their disease course. The combination of psychosis, trauma, and SLE as simultaneous facets of one hospital presentation makes JL’s case especially unique. This case demonstrates that while first-onset psychosis may herald a primary disorder, it may also represent one symptom of an underlying disease process. The treatment approaches to trauma spectrum disorder, NPSLE, and primary psychosis differ significantly; for example, while steroids may exacerbate schizophrenia and other primary psychotic disorders, they are a mainstay of treating NPSLE. Therefore, this case exemplifies the critical importance of distinguishing between the medical and psychiatric contributors to an individual patient’s presentation.
Mini Incision 24 Hour Rapid Recovery Augmentation Mammaplasty

BACKGROUND
For women interested in having breast augmentation, both perioperative and postoperative morbidity must be taken into consideration to facilitate the recovery process, and to provide for a remarkable cosmetic result. This study focused on meticulously refining surgical technique to significantly reduce postoperative pain/nausea, reduce recovery time/time required to return to normal activity, and to enable the patient to regain full strength quicker. Application and mastery of this surgical technique when approaching the breast augmentation procedure should not only decrease postoperative morbidity, but should significantly reduce the revision rate and capsular contraction occurrence in these patients.

METHODS
Surgical tissue trauma, such as tugging/pulling and unnecessary trauma to the underlying muscle directly influences the patient’s postoperative experience. Once an incision is made, prospective preparation for bleeding is imperative in order to accurately assess the condition of the pectoralis muscle and inframammary subpectoral pocket. Following the creation of the pocket using monopolar electrocautery dissection only, minimal release of the muscle should be performed from the three o’clock to the six o’clock position. Simultaneous meticulous hemostasis must be achieved with minimal tissue trauma during dissection, while also minimizing any blood that develops within this pocket. Precise visualization of the dissection minimizes the risk of compromising rib perichondrium or other sensitive anatomical structures within the vicinity. Pocket dimension assessment and demarcation of the lateral pocket limits enables the surgeon to visualize how the implant will situate. The use of powder-free gloves during the procedure is crucial to help drastically reduce the risk of capsular contraction postoperatively. The implants must be introduced into the pocket gently, so as to reduce any excessive tissue trauma or bleeding. The medications given preoperatively and intraoperatively by the anesthesiologists help to control pain level and postoperative nausea. By concomitantly mastering analgesic control and limiting postoperative nausea, postoperative morbidity is reduced.

RESULTS
Questionnaires pertaining to the patient’s postoperative experience have been distributed to a group of patients (females, 18 years of age) who have had surgery within the last year. The data is still being tabulated and finalized at this time.

CONCLUSIONS
A significant improvement in cosmesis and postoperative healing is likely to be achieved by even practiced surgeons if their technique is both re-evaluated and tailored appropriately using this particular rapid recovery methodology. Surgical efficiency coupled with medical proficiency and the ability to refine operative technique could provide for a superior cosmetic result, fewer postoperative complications, and lower revision rates.
Structure of Central Optic Disc Pit using Enhanced Depth Imaging Optical Coherence Tomography

OBJECTIVE
To evaluate the physical characteristics of central optic disc pits (ODPs) using enhanced depth imaging optical coherence tomography (EDI OCT).

DESIGN
Prospective, observational study.

PARTICIPANTS
15 eyes of 10 patients (mean age, 62.9 ± 19.7 years) with central ODPs and 2 eyes of 2 patients (39 and 64 years old) with no central ODPs or other ocular diseases were recruited.

METHODS
Serial horizontal and vertical EDI OCT images of the optic nerve complex (ONC) were obtained from both eyes of each participant. Deep ONC structures including lamina cribrosa (LC), short posterior ciliary artery (SPCA), central retinal artery (CRA) and vein (CRV), peripapillary choroid and sclera, and subarachnoid space around the optic nerve were investigated for their visibility and morphology.

MAIN OUTCOME MEASURES
The structure of a central ODP.

RESULTS
Central ODPs are full thickness defects in the LC.

CONCLUSIONS
EDI OCT revealed that central ODPs are full thickness defects in the LC and can be classified into 3 types depending on their spatial relationship to the LC pore for the CRVT.
BioDigital Systems, LLC in collaboration with New York University Langone Medical Center Department of Reconstructive Plastic Surgery has created an interactive, step-based latissimus musculocutaneous flap simulator. Preliminary testing of fourteen residents (PGY1-6) demonstrates that simulator training results in significant improvement in an objective assessment of surgical knowledge (p < 0.0006, pre-training score: 81.0%, post-training score 92.7%). This study is the first in the field of plastic and reconstructive surgery to demonstrate objective improvement in surgical knowledge as a result of simulator training, suggesting the potential effectiveness of simulators for a panoply of breast reconstruction options.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Prospective Blinded Laboratory Assessment of Prophylactic Antibiotic Compliance in a Pediatric Outpatient Setting

BACKGROUND

The American Urology Association guidelines suggest that pediatric patients diagnosed with vesicoureteral reflux (VUR) be placed on continuous antibiotic prophylaxis (CAP) in attempt to prevent ascending urinary tract infections (UTI) that can lead to renal scarring. While CAP is commonly prescribed in ambulatory care settings to impede the development of UTIs, it is important to note that patient non-adherence to recommended regimens is a perpetual issue. Compliance rates for patients diagnosed with VUR and prescribed prophylaxis have been shown to be as low as 40%. If the patients are truly non-compliant than surgical treatment of VUR would seem to be a more plausible option as any potential renal scarring would be avoided.

To our knowledge we conducted the first prospective, single blinded study that definitely assessed compliance by measuring antibiotic levels. Although compliance has been well studied in pediatric patients, prior studies for UTI prophylaxis have focused on using indirect methods such parental questionnaires and pharmacy claims data. Urine test help establish a more concrete perception of compliance as subjective measurements tend to be inflated.

METHODS

Children aged 0-18 years taking trimethoprim prophylaxis were recruited to partake in the study. The subjects were previously unaware of the study and approached to be enrolled during follow-up appointments. Urine samples were collected and antibiotic levels were quantified using chromatography.

RESULTS

Of those approached, 97% consented to participate (total n=54). The adherence rate was found to be 91%. Age, sex, self-report of compliance, duration of time on antibiotics, insurance status, history of breakthrough infection, surgery, pyelonephritis and hospitalization were not associated with compliance.

CONCLUSION

Our compliance rate of 91% contradicts much of the reported values for the treatment of UTIs in the pediatric population. The referral by a primary care provider to a surgeon might facilitate compliance because the seriousness of the condition becomes more apparent, especially as it made clear that poor adherence will likely result in the need of surgery. Furthermore, a specialist can focus on a single issue for the duration of the entire visit to ensure that better parental clarity and understanding is achieved as compared to a primary care setting where multiple issues demand attention. Future studies should measure compliance in both other sub-speciality and general pediatric clinics. If adherence can not be established, perhaps pediatric urologists should be more involved with the care regardless of the future likelihood of surgery.
Intra-arterial Access: Stuck With One Limb

Due to easy accessibility and collateral circulation, the radial artery is generally the primary site for invasive arterial line placement. However, certain circumstances and patient comorbidities may make radial artery cannulation difficult.

This case is of a 68-year-old man with history of extensive vascular disease and bilateral femoral bypass stents who presented to the ER with left-sided stroke due to significant right sided carotid plaque. CT angiogram also showed 90% stenosis of the left subclavian artery. The patient was scheduled for right carotid endarterectomy.

Given the nature of the surgical procedure, intra-arterial blood pressure monitoring was part of the plan. Pre-induction, several unsuccessful attempts were made for arterial line access at the right radial artery. The left radial artery was not considered an option due to stenosis of the left subclavian artery as seen on CT angio. The femoral arteries were not an option given the patient’s prior surgical history. In addition, the patient did not have palpable dorsalis pedis pulses. The decision was made to place an arterial line in the patient’s right axillary artery under ultrasound guidance.

Some anesthesia cases or patients in the ICU require invasive BP monitoring. Due to prior medical history, surgical history or planned surgical case, there may be limits to available sites for arterial access. Alternative sites of access should be considered with site-specific complications taken into account. Alternative techniques should be taught and practiced for these cases.

In addition, the value, evidence and absolute need for arterial monitoring during carotid endarterectomy surgery should be recognized. Contraindications and challenges associated with axillary arterial line placement should be discussed.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Combined Ablative and Non-Ablative Fractional Treatment For Facial Skin Rejuvenation

BACKGROUND
Coagulation and residual thermal injury are limiting factors for maximizing single treatment coverage of fractional deep treatments. A new strategy to combine the coagulate damage from non-ablative fractional treatment with fractional ablative treatment was evaluated in an ex vivo model for skin shrinkage and in a clinical study for facial skin rejuvenation.

METHODS
Facial skin from rhytidectomies was treated using the Lux2940, Lux1540, and/or Lux1440 (Palomar, MA) micro-fractional hand pieces under controlled conditions. Tissue shrinkage was quantified as a function of depth and density of fractional treatment. Safety, side effects, and effectiveness with a minimum of 3-month follow-up were evaluated in 18 patients for facial rejuvenation with combined non-ablative and ablative coverage reaching over 50%.

RESULTS
Skin tightening was observed in the ex vivo model that was directly proportional to both density and depth of treatment. When combined, the ablative and non-ablative effects were additive yielding up to 30% shrinkage. At similar settings, patient treatments were well-tolerated with only topical anesthesia, had minimal bleeding and re-epithelialized within 4 days. Combination high coverage (25% plus 25%) single treatments at < 300 micrometer depths resulted in over 75% improvement in skin texture, fine lines, and pigmentation with acceptable side effects and downtime compared to lower coverage fractional ablative only treatments. Combination treatments with column depths up to 1 mm achieved over 50% reduction in wrinkles and notable reduction in facial laxity.

CONCLUSION
Combined fractional non-ablative and ablative treatment made higher single treatment coverage (50%) possible and resulted in greater effectiveness than either modality alone. Combining these modalities offers new strategies for skin rejuvenation which helps manage side effects and the downtime associated with ablative-only procedures.
Sedation Level During Outpatient Ketamine Infusions for Chronic Pain

OBJECTIVES/BACKGROUND

Ketamine is an NMDA receptor antagonist that may reduce severe debilitating pain in chronic pain patients unresponsive to conventional treatment modalities. Ketamine is an anesthetic and has been shown to have a wide range of effects in humans including sedation, hallucinations, bronchodilation, elevation of blood pressure and heart rate, and analgesia. The goal of our study is to determine whether ketamine has a significant effect on the level of sedation during continuous infusion of the drug over 4 hours in an outpatient setting.

METHODS

With IRB approval, we reviewed the sedation scores of 46 patients with chronic neuropathic pain or complex regional pain syndrome (CRPS). The patients underwent 3 consecutive days of 4 hour ketamine infusions each day with a dose increase each day. The patients were monitored in the PACU at the GWU Ambulatory Surgery Center. Each patient received a baseline Sedation-Agitation Scale (SAS) score, and every 15 minutes during the infusion, and prior to discharge home. Patients received midazolam 2 mg prior to the start of the infusion and additional midazolam as needed, for restlessness, up to a total dose of midazolam 8 mg. All patients were observed for at least an hour after completion of ketamine infusion before discharge home.

RESULTS

A total of 138 ketamine infusions were administered. The dose of ketamine ranged from 0.2 to 1.2 mg/kg/hr calculated to a total dose for 4 hours. The total dose of ketamine administered each time ranged from 36 mg to 510 mg. All patients had a baseline SAS score of 4 (calm, cooperative). The lowest SAS score for all patients during the infusions, was 3 (sedated, arousable to verbal stimuli or gentle shaking, follows simple commands but drifts off again). There was no significant increase in sedation with increased ketamine dose or intermittent administration of midazolam. Sedation score returned to baseline in all patients upon discharge.

CONCLUSIONS

Outpatient ketamine infusions are associated with increased sedation from which patients are easily aroused. Sedation level during infusion was not influenced by ketamine dose or intermittent administration of midazolam. All patients returned to baseline sedation level upon discharge. Continuous 4 hour infusions of ketamine at subanesthetic doses may be safely administered to outpatients for management of severe chronic neuropathic pain.
Local Anesthetic Resistance in a Laboring Parturient

BACKGROUND
A healthy 36 year-old G4P1 parturient presents for labor at term of an uncomplicated pregnancy. She has a history of insensitivity to local anesthetics (LAs) during dental procedures. She had no pain relief during her previous labor when bupivacaine/lidocaine were used in the epidural catheter despite replacement of the catheter to rule out misplacement and numerous episodes of rebolusing with LAs. She confirms a family history of similar insensitivity.

METHODS
Many labor analgesia options were discussed with the patient including re-attempting an epidural, placing a spinal or a combined-spinal epidural (CSE) using fentanyl in the intrathecal space, or starting a remifentanil patient controlled analgesia (PCA). In the event that instrumentation was necessary for a vaginal birth, the patient would be administered nitrous oxide in the operating room. In the event of an emergent Cesarean section, the patient would be placed under general anesthesia.

RESULTS
After discussing the risks and benefits and obtaining informed consent, a CSE was performed using intrathecal fentanyl from which the patient received good pain relief for 2.5 hours. At that point, her block regressed, and she received lidocaine, an amide LA, in the epidural catheter. She did not get a response, and chlorprocaine, an ester LA, was administered in the epidural catheter, which provided adequate pain control. She was bolused several times and, eventually, a chlorprocaine infusion was started for the duration of her labor. Eight hours after placement of the CSE, a C-section was performed due to failure to progress. It was performed under general anesthesia without complications.

CONCLUSIONS
When epidural anesthesia does not work, it is usually attributed to technical failure. Anesthesia providers very rarely encounter patients with LA insensitivity, although some cases have been reported. Local anesthetics work by blocking sodium ion channels in the cell membrane, and it is possible that mutations in these channels could result in full or partial resistance to these drugs. It is interesting to note that while our patient had a known insensitivity to LA, it was specific to the amide class and she had a partial response to ester class, something that has not been noted in the literature. Insensitivity specific to the amides could be attributed to differences in molecular structure as compared to the esters. In summary, the mechanism of LA insensitivity is unknown but may be class specific, and clinicians can circumvent this insensitivity by switching to another LA class of drugs.
Antithrombin III Deficiency in a High-Risk Parturient with Twin Gestation

INTRODUCTION
Pulmonary embolism remains one of the most common causes of maternal death due to the hypercoaguable state of pregnancy. Antithrombin III (AT III) is a protease inhibitor that lyses factor Xa and thrombin. AT III deficiency increases the chance of thrombosis by 60% during pregnancy and 33% in the puerperium period.¹ This case describes a parturient with AT III deficiency on Thrombate, an AT III concentrate, and anticoagulation therapy, complicating the administration of neuraxial anesthesia. A literature review revealed one prior case report of Thrombate use prior to neuraxial anesthesia administration.²

CASE DESCRIPTION
A 36 year-old G₁,P₀ at 33⁵ weeks gestational age with twins presented for an elective primary Cesarean section. The patient was incidentally diagnosed with AT III deficiency. She had no other symptoms or known thromboembolic events, and was otherwise healthy. She was treated prophylactically with Lovenox 40 mg SC BID and aspirin 81 mg PO daily. She received Lovenox 24 hours prior to admission. Laboratory findings revealed normal CBC and coagulation panel. Physical exam was notable for Mallampati class II airway and grossly normal spine amenable to neuraxial anesthesia. One hour prior to the surgery, she received Thrombate 2000 IU IV per her Maternal-Fetal Medicine provider recommendation, as transfusion of fresh frozen plasma (FFP) would not raise her AT III levels sufficiently. After explaining the anesthetic risks of neuraxial blockade (including increased risk for bleeding) and obtaining informed consent, a single shot spinal was placed atraumatically in the L₂-L₃ interspace using bupivacaine 12 mg, fentanyl 20 mcg, and morphine 300 mcg for postoperative pain control. The procedure proceeded uneventfully and Lovenox was resumed 24 hours after the C-section. Her block receded 3 hours after placement and baseline neurologic function returned. She did not develop any evidence of epidural hematoma.

DISCUSSION
This case illustrates the use of Thrombate in the setting of neuraxial blockade, of which there is very little experience. It is unclear if Thrombate increases the risk of bleeding, but in this patient, the administered dose would, theoretically, only raise AT III levels to low-normal. We followed the American Society of Regional Anesthesia (ASRA) guidelines and deferred needle placement 24 hours after the last Lovenox dose. In addition, we chose spinal anesthesia, which uses a smaller needle and thereby decreases the risk for trauma and bleeding, as opposed to epidural anesthesia.¹ Further research is needed to provide recommendations for safe neuraxial anesthesia when administering Thrombate.
Peripheral laser iridoplasty opens angle in plateau iris angle closure by thinning the cross sectional iris as imaged by anterior segment spectral domain optic coherence tomography (SD-OCT).

**Purposes**
To evaluate the mechanism of angle closure in plateau iris before and after laser iridoplasty as imaged by anterior segment SD-OCT.

**Methods**
A 28 y.o. Caucasian female with history of narrow occludable angles OU and laser peripheral iridotomies OU one year prior, presented with acute angle closure glaucoma (IOP 26mm Hg OD, 31mmHg OS). High-frequency ultrasound biomicroscopy (UBM) confirmed the anterior location of the ciliary processes. Anterior segment SD-OCT images were taken at 3, 6, 9 and 12 o’clock of the angle of each eye before and after laser iridoplasty.

**Results**
The anterior segment SD-OCT demonstrated angle closure with elevated IOP even with patent iridotomies. Laser peripheral iridoplasty was performed in each eye. Gonioscopy after laser peripheral iridoplasty revealed angles open to scleral spur (valleys) in the areas of iridoplasty and closed in the untreated areas. The anterior segment SD-OCT demonstrated iris thinning in the areas of treatment. Iris cross sectional thickness was 278 µm in the iridoplasty treated areas compared with 315 µm in the closed untreated areas (p=0.007).

**Conclusions**
Plateau iris is a unique subtype of angle closure glaucoma. It is commonly caused by anteriorly positioned ciliary processes that push the peripheral iris forward, resulting in angle closure. Anterior segment SD-OCT demonstrated iris cross sectional thinning as the mechanism of opening the angle in plateau iris angle closure treated by laser iridoplasty.
Continuous Data Acquisition During Mechanical Ventilation: A Longitudinal Study

OBJECTIVES

There are no longitudinal studies in which patient data have been acquired continuously. To this end we developed a computerized data acquisition system to collect and store ventilator and hemodynamic data during the entire duration of mechanical ventilation.

METHODS

Prospective, observational study of adult critically ill patients enrolled within 24 hours of initiation of mechanical ventilation. Hemodynamic and ventilator data were acquired at 30 Hz and analyzed at 2.5 min intervals. Patients were studied from enrollment to weaning or to ICU discharge. Demographic data and diagnosis leading to intubation were recorded as were complications (e.g. barotraumas, re-intubation) and 28-day mortality.

RESULTS

We enrolled 140 patients aged; 53% were male. 28-day mortality from all causes was 25.7%. We monitored patients for 53 [21-153] hours (min 1hr; max 1100 hr). There was a higher incidence of sepsis in decedents (16.7% vs. 2.9; p<0.01); odds ratio 6.7 (1.6-28.6). There were no differences in ventilator associated pneumonia (22% vs. 27%), barotrauma or weaning failures. Shown are the median [IQR] of each patient’s average measurements taken during the observation period.

<table>
<thead>
<tr>
<th></th>
<th>Combined</th>
<th>Survivors</th>
<th>Decedents</th>
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<tbody>
<tr>
<td>Ventilation (d)</td>
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<td>4[3-7]</td>
<td>6[3-8]</td>
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<td>8[5-15]</td>
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<td>17[9-28]</td>
<td>10[5-22]</td>
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<td>56[46-69]</td>
<td>71[55-81]</td>
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<td>5[4-8]</td>
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<td>40[40-45]</td>
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<td>Mean RR (bpm)</td>
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<td>20.5[17.5-24.0]</td>
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<tr>
<td>Mean MeanP (cmH2O)</td>
<td>10.2[8.9-12.5]</td>
<td>9.9[8.4-10.8]</td>
<td>14.4[10.7-16.6]</td>
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<tr>
<td>Mean PEEP (cmH2O)</td>
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<td>5.1[4.7-5.8]</td>
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<td>Mean TV (mL/kg)</td>
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<td>MV (L/min)</td>
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<td>8.0[6.9-9.4]</td>
<td>10.4[8.3-11.8]</td>
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</table>

LOS= Length of stay; RR= Respiratory rate; MeanP = Mean airway pressure; TV= Tidal volume; MV = Minute volume. * p < 0.05; † p<0.01

CONCLUSIONS

In this cohort of mechanically ventilated patients, survivors were younger, less sick and required lower FIO2, RR, MeanP and MV than decedents. Sepsis was an independent risk factor for mortality.
The Effect of Advanced Age on Survival in Mechanically Ventilated Patients

OBJECTIVES

Few studies have evaluated outcome in older patients undergoing mechanical ventilation. Our aim was to assess the relationship between advanced age and outcome in mechanically ventilated patients.

METHODS

Prospective observational study of critically ill adults enrolled within 24 hours of initiation of mechanical ventilation. Demographic data and diagnosis leading to intubation were recorded; SAPS and SOFA scores were calculated. Patients were followed for 28 days after initiation of mechanical ventilation to evaluate length of ICU and hospital stay, duration of mechanical ventilation, and 28-day mortality.

RESULTS

140 patients were enrolled. Of these, 23 (16.4%) were between 70 and 80 years old and 24 (17.1%) were >80 years old. The use of mechanical ventilation was directly related to patient age (r² = 0.40). Mortality increased up to age 70 with no differences noted between patients in the 8th and 9th decades of life. There was a trend towards increased mortality in African Americans (p = 0.21). There were no differences in ICU or hospital length of stay according to age.

CONCLUSIONS

The number of elderly patients undergoing mechanical ventilation is increasing. Our data suggest that mortality in these patients is no longer a function of age past 70 years. This finding should be taken into consideration when assessing the need for mechanical ventilation in the very old.
Cancer Survivorship Care: A needs assessment for curriculum development in resident education

NEEDS AND OBJECTIVES

There are nearly 12 million cancer survivors in the United States. With ongoing innovations in cancer treatment, that population will grow to approximately 20 million by 2020. As the surviving population ages, who should oversee medical care for cancer survivors—internists or oncologists? Based upon prior surveys, oncologists feel comfortable with survivorship care, but lack the time and resources to provide long-term survivorship care to millions of patients; general internists, however, feel that they lack adequate knowledge and confidence in providing survivorship care. To date, internal medicine residents have not been assessed regarding their attitudes towards cancer survivorship care.

Our unique survey was intended to assess the knowledge and attitudes of internal medicine residents towards survivorship care to prepare for the implementation of a survivorship residency curriculum. This longitudinal curriculum is aimed at increasing internal medicine residents' awareness of long term effects and their confidence in treating cancer survivors.

SETTINGS/PARTICIPANTS

All internal medicine residents at George Washington were asked to complete an IRB approved survey during a town hall meeting in July 2011.

DESCRIPTION

A 10-item questionnaire was provided to assess the knowledge and attitudes of internal medicine residents on survivorship care. This survey included demographic information (PGY level, residency tract) as well as likert scale questions designed to assess the interest and confidence in providing survivorship care to patients in their practice.

EVALUATION/RESULTS

Seventy-two (70%) of the internal medicine residents completed the survey. Overwhelmingly primary care (100%) and non-primary care bound (76%) residents felt cancer survivors should receive their long-term care from both hematologist/oncologist and internists. Of those surveyed, 99% stated they were interested in learning how to provide survivorship care to their patients; however, only 61% indicated they would feel comfortable monitoring for late and long-term effects in cancer survivors. In addition, 50% of respondents stated they were familiar with late effects of cancer treatment. Finally, 37% stated they were familiar with resources or support services for cancer survivors.

DISCUSSION

There is a growing need to provide long-term cancer survivorship care to millions of survivors. Based on our questionnaire results, internal medicine residents are motivated to participate in the care of cancer survivors; however, they appear to lack the knowledge and confidence to provide this care. Our results are consistent with the survey results of practicing internists who also feel they lack adequate knowledge and confidence in survivorship care.

Background studies establish the need for cancer survivorship education. Our results suggest that a collaborative effort between internists and oncologists would be the preferred model for resident education. In sum, our study shows that a cancer survivorship curriculum should be part of resident education to train future internists who will be providing long-term care to our rapidly growing population of cancer survivors in the United States.
The Effect of Pan-Retinal Photocoagulation on Macular Inner Retinal Thickness in Proliferative Diabetic Retinopathy

**Purpose**
Panretinal photocoagulation (PRP) for patients with proliferative diabetic retinopathy (PDR) improves visual outcomes and prevents vision loss. Studies using Time-Domain Ocular Coherence Tomography (TD-OCT) have shown an increase in edema and overall macular thickness following the procedure, but the TD-OCT lacks the resolution to accurately measure the individual layers of the retina. It has not yet been investigated using Spectral-Domain OCT (SD-OCT) whether certain layers of the retina may thin even while overall thickness may increase.

The purpose of this study is to conduct a retrospective analysis on patients with PDR who have undergone PRP and had SD-OCT before and after the procedure to determine the change in thickness of the retinal layers after treatment at 1, 3, and 6 month intervals.

**Methods**
All 99 patients with PDR who underwent a total of 202 sessions of PRP over a 2 year period were identified using the electronic medical record. Of these, 27 eyes from 18 patients met the criteria for inclusion, including no prior PRP, scans at the appropriate intervals using SD-OCT, and clarity of optical media to permit adequate quality scans. Baseline scans were obtained before PRP, then at 1, 3, and 6 months following. All patients were scanned using the Optovue RTVue system and scans were analyzed to determine the total, inner or “ganglion cell complex,” and outer retinal thickness; each measurement was taken at the fovea, 1.5mm (parafoveal) and 3mm (perifoveal) from the center. Additionally, charts were reviewed to determine visual acuity, number of laser spots, years since diagnosis of diabetes, age, sex, race, and presence of CSME or glaucoma.

**Results**
Ages ranged from 35-75 years; the average age was 54. 89% were African-American and 11% were Hispanic. The baseline average total central foveal thickness was 282.96µ; this increased at the 1 month visit, then decreased at the 3 month (258.58µ) and 6 months visits (234.88µ; p=0.061). Total parafoveal thickness and perifoveal thickness did not change significantly. Average central inner retinal thickness decreased from a baseline 85.8µ to 71.3µ at 6 months (p=0.101). Average central outer retinal thickness decreased from 197.12 µ to 163.55 µ at 6 months (p=0.093). Patients with CSME showed a 12.7% decrease in total thickness at 6 months, while patients without showed a 20.67% decrease in total thickness.

**Conclusions**
The inner and outer retinal layers both decrease in thickness over the 6 months following PRP in a pattern that trends towards but does not meet statistical significance. Interestingly, this trend is seen in patients both with and without CSME, suggesting that the thinning effect is independent of resolution of concurrent macular edema.
A Systematic Review Of The Efficacy Of Tricyclic Antidepressants For Cyclic Vomiting Syndrome

BACKGROUND
Cyclic vomiting syndrome (CVS) is a functional gastrointestinal disorder that ranges in severity from mild to severely debilitating. Long thought to be a disease of pediatrics, CVS is now known to be a disease that can affect any age group. The incidence of CVS appears to be increasing and a recent study suggests that patients with CVS have high rates of utilization of ED service. (1) Delay in diagnosis results in impaired quality of life due to difficulty maintaining employment and increased healthcare utilization. (2) Tricyclic antidepressants are a promising pharmacologic therapy for CVS.

OBJECTIVE
The purpose of this systematic review is to determine the efficacy of TCAs in adult patients with CVS for prophylactic therapy.

METHODS
Using the Population, Intervention, Comparison, and Outcome (PICO) format, we broke down the research question into the following parts: (1) Population: Adult human subjects with CVS; (2) Intervention: TCA pharmaceuticals; (3) Comparison: Observation (when available); (4) Outcome: Resolution or mitigation of CVS, negative outcomes of medication. The primary search strategy was a PubMed database query (1985 to 2011) to identify articles that investigated treatment of adults for CVS. Our MEDLINE search strategy linked terms abdominal migraine, recurrent vomiting, functional vomiting, cyclic vomiting syndrome, vomiting syndrome, vomiting recurrence and cyclic (1985-2011) with the Boolean operator “AND”. Results were limited to human subjects and English language. The MEDLINE terms were then modified to approximate set of equivalent terms to be used to search the Scopus Sciverse database (1985 to 2011) and the Cochrane Library (1900 to 2011). To find unpublished data, electronic searches of clinical trials.gov and current controlled trials and National Health Service-The National Research Register were conducted. Experts in the field were also contacted to discover any unpublished studies. Studies were excluded if they focused solely on pediatric patients or did not describe a TCA therapy.

RESULTS
7 studies enrolled a total of 419 subjects to test the effectiveness of TCA administration for CVS. All studies were open-labeled and lacked a control. In summary, a favorable outcome was observed in 80% of patients who were treated with TCAs. 21% of patients reported unfavorable outcomes which ranged in severity from dry mouth to hallucinations. Average follow-up of patients was 21 months.

DISCUSSION
Our systematic review has demonstrated the potential benefit for TCAs in the treatment of CVS. Future studies are urgently required with robust methodology and control comparison.
TREATMENT OF KYPHOSCOLIOSIS IN PROTEUS SYNDROME: CASE REPORT AND REVIEW OF THE LITERATURE

OBJECTIVES
Present a case of severe kyphoscoliosis associated with Proteus syndrome (PS) and review orthopaedic literature on management of scoliosis and kyphosis in PS in order to address safety and efficacy of surgically correcting spinal deformity in PS.

BACKGROUND
PS is a rare disorder of mosaic growth dysregulation involving hamartomatous overgrowth caused by a non-hereditary, somatic mutation. Aggressive, irregular overgrowth is the hallmark of PS. Orthopaedic issues associated with the disorder include local gigantism, hemihypertrophy of various systems, exostoses, limb-length discrepancy, angular deformities, macrodactyly, macrocephaly, kyphosis, and scoliosis.

METHODS
A male patient was followed from the age of 11 to the age of 15 and received surgical treatment for progression of severe kyphoscoliosis associated with PS with posterior spinal instrumentation and fusion. The existing literature on treatment of spinal deformity in PS was reviewed to characterize optimal treatment options.

RESULTS
The limited existing literature discussing orthopaedic management of spinal deformity in PS has demonstrated difficulty in attaining lasting curve stabilization. In addition to persistent difficulties in treating spinal deformities, unpredictable tissue reactions to surgery and complicating blood loss and thromboses have been documented in PS. We hypothesized that use of current deformity correction strategies employing spinal osteotomies, thoracic pedicle screws, and vertebral de-rotation maneuvers would provide more rigid multi-column fixation, improve correction, and lower risk of deformity recurrence. Our patient was satisfactorily corrected from scoliotic curves of 65° to 17° at C6-T5, 88° to 39° at T5-T10, 41° to 20° at T10-L4, and from a kyphotic curve of 92° to 65° at T3-T10 with no complications and his correction remains stable one-year post-operatively.

CONCLUSION
To our knowledge, this is the first reported case of current deformity correction strategies employing spinal osteotomies, thoracic pedicle screws, and vertebral de-rotation for the correction of the kyphoscoliosis associated with PS. Pre-operative MRI screening for paraspinal tumors, consultations from hematology, cardiology, and pulmonology, DVT prophylaxis, and intra-operative spinal cord monitoring are essential for orthopaedic management of spinal deformity in PS.
Long-Term Outcome and Quality of Life in Crohn’s Disease Patients After Fecal Diversion

INTRODUCTION

Although total proctocolectomy is the surgical standard of care, fecal diversion using an ileostomy or colostomy alone is used selectively in cases of Crohn’s colitis refractory to medical treatment. However, long-term effectiveness and health-related quality of life (HRQOL) of Crohn’s disease (CD) patients that have undergone fecal diversion is not well defined.

OBJECTIVE

Measure the long-term effectiveness and HRQOL of CD patients having undergone a diverting ileostomy or colostomy without synchronous bowel resection.

METHODS

CD patients involving the colorectum and/or those with perianal disease operated on by a single surgeon were identified by chart review. Demographic, disease, and surgical characteristics were tabulated. HRQOL using the Short Form 36 (SF-36) Health Survey was assessed at last followup using a webtool. Significance of differences in SF-36 scale scores between CD patients undergoing fecal diversion and the general U.S. population data with the chronic diseases irritable bowel disease (IBS) and diabetes mellitus (DM) was estimated using t statistics with comparisons being adjusted for the general population mean of SF-36 scale score with the appropriate age and gender subgroup.

RESULTS

The study cohort of 34 patients had a median age of 33 years (range, 15-92) and included 18 (53%) males. Fecal diversion was accomplished using an ileostomy in 31 patients (91%) or colostomy in 3 patients (9%). Indications for fecal diversion were perianal disease (n=27) and refractory Crohn’s proctocolitis (n=7). After a median followup of 4 years (range, 1-10) after surgery, 9 (26%) required additional procedures for continuing symptoms arising from bowel distal to the stoma, including total colectomy (n=4), proctocolectomy (n=2), both colectomy and proctocolectomy (n=1), and abdominal perineal resection (n=2). Twenty-three patients have been controlled using a combination of drugs, including steroids (n=9), immunomodulators (n=9) and biologics (n=5). The remaining two patients were asymptomatic and not on any medications. Twenty-two patients (65%) completed the survey. On all 8 SF-36 scales, CD patients had significantly worse HRQOL than the U.S. general population (p< 0.001). Compared with DM patients, there was no significant difference in mean SF-36 score on all SF-36 scales except social functioning (p < 0.001). CD patients had no significantly worse HRQOL on all SF-36 scales compared to patients with IBS.

CONCLUSION

Approximately 25% of CD patients undergoing fecal diversion for refractory perianal disease or proctocolitis require further resectional therapy of distal bowel. Although HRQOL was significantly lower in CD patients undergoing fecal diversion than in healthy population, overall HRQOL was not significantly different from patients with other chronic diseases such as DM or IBS.
The Combined Use of BMP 2 and BMP 7 in Complex Revision and Reconstructive Spine Surgery

STUDY DESIGN
A retrospective review of 27 consecutive patients who received a combination of BMP 2 and BMP 7 in a revision posterolateral lumbar fusion.

OBJECTIVE
To determine the prevalence of short-term complications associated with using BMP 2 in synergy with BMP 7 in posterolateral lumbar fusion.

SUMMARY OF BACKGROUND DATA
Prior clinical studies have established the safety and efficacy of BMP 2 and BMP 7 when used independently in posterolateral lumbar fusions. In vitro studies have demonstrated synergistic properties when BMP 2 and BMP 7 are combined. To date, there are no reports detailing the in vivo safety of combining BMP 2 and BMP 7 in posterolateral lumbar fusion.

METHODS
We performed a retrospective review of 27 patients who received BMP 2 and BMP 7 in posterolateral lumbar fusions. Patients were followed for an average of 10.9 months. Medical records were used to determine the prevalence of post-operative complications such as infection, inflammation, hematoma, nerve damage, ectopic bone formation, and hypersensitivity reactions.

RESULTS
26 (96%) of 27 patients showed no short-term post-operative complications associated with the combined BMP 2 and BMP 7 implant. One patient developed an infection at the surgical site that was successfully treated with antibiotics. There were no other cases of adverse events.

CONCLUSION
Combining BMP 2 and BMP 7 in a posterolateral lumbar fusion presents a minimal risk of surgical complications. This combined therapy presents a new and innovative approach to posterolateral lumbar fusions.
Colorectal cancer causes significant morbidity and mortality in the United States. Guidelines for colorectal cancer screening are well accepted. Multiple factors affect adherence to recommendations. It has been suggested that African-Americans less frequently adhere to colonoscopy recommendations. This study evaluated the impact of patient race upon colorectal cancer screening when there is similar access to health care.

METHODS

The medical records of all patients referred for a colonoscopy from a primary care physician to a university gastroenterology practice during a 6 month period were evaluated. Patient age, gender and race were obtained. There were no exclusion criteria. A database, maintaining patient confidentiality, was created using Microsoft Excel. Statistical analysis was performed using a Fisher Exact test with significance set at p<0.05.

RESULTS

Six hundred patients (379 female, 221 male) were referred for a colonoscopy. There were 325 African-American, 138 Caucasian, 71 Hispanic and 66 did not have their race documented in the medical record. The mean age was 51 years. 309 of the 379 females (81.5%) and 174 of the 221 (78.7%) males underwent the recommended colonoscopy. There was no significant difference (p=0.4547) in the rate of colonoscopy compliance based upon gender. 265 of 325 (81.5%) African-Americans, 112 of 138 (81.1%) Caucasians and 55 of 71 (71.4%) Hispanics underwent the recommended colonoscopy. There was no significant difference in the rate of colonoscopy between African-Americans and Caucasians (p=0.2197) and Hispanics (p=0.0759). There was no significant difference (p=0.5856) in the rate of colonoscopy between Caucasians and Hispanics.

CONCLUSION

Colorectal cancer screening is a key component for decreasing the morbidity and mortality from the malignancy. Multiple factors impact upon adherence to colonoscopy. Patient race has been suggested to be a factor that can significantly influence compliance with medical recommendations. This study revealed that patient race and gender did not significantly influence the rate of colonoscopy compliance. It appears that patients who have access to care and come for health maintenance evaluations have similar compliance with colorectal cancer screening recommendations. Further study is necessary to determine key factors which impact upon colonoscopy screening.
Endoscopic management of skull base pathology requires a interdisciplinary surgical approach. A comprehensive knowledge of the extracranial and intracranial anatomy is critical to achieve successful outcomes and decrease complications. Surgeons must familiarize themselves with anatomy of the ethmoid region, lateral nasal wall, sphenoid sinus, cavernous region, sellar suprasellar region, clivus, and pterygopalatine/infratemporal fossa before embarking on these approaches.

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Children's National Medical Center has seen an evolution in wound care practices over the past decade, with negative-pressure wound therapy (NPWT) emerging as a critical modality. The purpose of this study was to analyze the use of NPWT at our institution, contrasting early NPWT use with current practice and identifying how NPWT use has varied based on patient age and wound etiology. Our initial review covered the years 2001-2007; the second was performed for fiscal year 2011. NPWT was used in 169 patients from 2001–2007 and in 92 patients in FY 2011. Our study confirmed the safe and effective use of NPWT from infancy to young adulthood for a variety of wound etiologies. NPWT has become the standard of care for split-thickness skin grafts at Children's National. It often allows closure without skin grafts in patients with large soft-tissue wounds. NPWT is most frequently used in burn patients, allowing significantly decreased length of stay. It also plays a crucial role in wound care of complex, high-risk patients with infected wounds following neuromuscular spine, abdominal, and cardiac surgeries. Finally, NPWT is also being used for indications not well defined in the literature, such as in primary osteomyelitis and soft-tissue infections.
Is Ehlers Danlos Syndrome a contraindication for Brachial Plexus Block?

Ehlers Danlos Syndrome (EDS) is a group of inherited genetic disorders of the connective tissue. Symptoms vary from mildly loose joints and lax skin to life threatening complications due to fragile blood vessels. Due to the presence of a defective collagen, anesthetic management in patients with EDS can be challenging. Only one previous case has been described on brachial plexus blocks in patients with Ehler Danlos syndrome.

CASE

Our patient was a 14 year old, active female, with documented EDS, who presented for a capsullorrhaphy of the left shoulder joint due to frequent subluxations. Preoperative evaluation revealed a history of easy bruising, normal cardiac imaging and normal lab work. A peripheral nerve block was selected for the anesthetic and adequate analgesia was obtained with an interscalene approach to brachial plexus block. The patient suffered no adverse complications such as hematoma, infection, or nerve injury and pain control was adequate throughout the perioperative period.

DISCUSSION

Regional anesthesia is an excellent method of relieving postoperative pain. Risks and benefits need to be considered before deciding to proceed with peripheral nerve blocks in patients who are prone to bleeding and nerve injury. Regional anesthesia can be a safe option in patients with EDS who are carefully selected based on the severity of symptoms.
Multiday Outpatient Ketamine Infusion for Chronic Visceral Hypersensitivity

BACKGROUND AND MIMS
Patients with functional gastrointestinal disorders may possess a lower threshold to visceral stimulus resulting in visceral hypersensitivity and frequent abdominal pain. One mechanism is thought to be NMDA receptor activation leading to central sensitization. We present a patient with persistent severe abdominal pain and gastroparesis who was treated with outpatient ketamine infusions.

METHODS
A 47 year old female diagnosed with diabetic gastroparesis since 2008 presents with worsening chronic abdominal pain and nausea unrelieved with medications and pyloric botox injections. She had temporary relief with a gastric stimulator and a prognostic celiac plexus block. Subsequent neurolytic block did not provide optimal relief. She underwent three consecutive days of outpatient ketamine infusions for four hours each day at an initial dose of 0.2mg/kg/hour, and increasing to 0.4mg/kg/hour and 0.6 mg/kg/hour on the third day.

RESULTS
The patient reported significant relief of abdominal pain and nausea for five weeks. The pain reduced from 6/10 to 0/10. There were no adverse side effects.

CONCLUSIONS
We present a case of intractable abdominal pain related to diabetic gastroparesis previously unresponsive to multiple modalities for pain control. The patient experienced a significant reduction in pain after outpatient ketamine infusions. Central sensitization through activation of NMDA receptors may play a role in visceral hypersensitivity. Ketamine, an NMDA receptor antagonist may be helpful in reducing persistent severe abdominal pain unresponsive to other treatments.
Outpatient continuous ultrasound guided transverse abdominis plane (TAP) block for management of chronic intractable abdominal pain

BACKGROUND

Chronic abdominal pain is not uncommon, and often incapacitating. Patients undergo extensive workup, but invariably end up without a definitive diagnosis. Many are treated with opioid analgesics, which produce undesirable side effects. We present two patients with chronic intractable abdominal pain, who experienced long term relief from continuous TAP block. DT is a 58 year old female with intractable abdominal pain in the left upper quadrant of unknown etiology for 20 years, and a history of multiple surgeries. She rates her pain 8/10, which is unrelieved with oral or topical analgesics, trigger point injections, celiac plexus blocks, or peripheral stimulation. Intercostal blocks provided slight relief, while a single TAP block provided significant, but temporary relief. SW is a 61 year old female with chronic intermittent abdominal pain for 40 years. Her history includes two abdominal surgeries, irritable bowel syndrome, and diabetic gastroparesis. She reported increasing pain in her left abdomen the past two years, with some relief from opioids. A single left TAP block decreased her pain score from 8/10 to 5/10.

METHODS

A catheter was placed in the transverse abdominis plane using ultrasound guidance. After a bolus of ropivacaine 0.35% or 0.5%, a continuous infusion of ropivacaine 0.2% at 4cc/hour was started. Each patient was discharged home, phoned daily, and the catheter was removed several days later.

RESULTS

DT had decreased pain scores to 3/10, and reported good relief for 5 weeks. Continuous TAP block was repeated several months later with decrease in pain score to 0/10 for 5 weeks. SW reported decreased pain scores ranging 2-4/10. She continued to report pain relief 8 to 9 weeks later, and minimal use of opioids. Neither patient had complications or adverse side effects.

CONCLUSIONS

The exact etiology of chronic abdominal pain was not fully determined in either case, but somatosensory pain likely played a significant role. The external and internal obliques, and the transversus abdominis muscles make up the anterolateral abdominal wall, which is innervated by ventral rami of the thoracolumbar nerves- T6 to L1. These nerves lie in the TAP between the internal oblique and transversus abdominis muscles, and can be blocked by local anesthetics resulting in analgesia of the abdominal wall. Both patients experienced significant pain relief, lasting 5-9 weeks, without adverse side effects. Continuous TAP blocks, placed under ultrasound guidance, may offer relief for a period of time in chronic intractable abdominal pain of somatosensory origin.
Anesthetic Considerations for Excision of a Chest Mass

OBJECTIVES
This is a case report of a surgical operation of an excision of a chest mass, with emphasis on anesthetic concerns.

BACKGROUND
A 45 year old male presented to the operating room for excision of a chest mass. The patient was otherwise healthy with no significant medical history. Initially the patient had presented with hemoptysis. Initial biopsies were inconclusive. On imaging, the mass was found to be in the pulmonary veins extending to the left atrium. The patient was scheduled for a left thoracotomy, resection of tumor, possible pneumonectomy, with fem-fem bypass.

RESULTS
The patient successfully underwent surgery, including intubation with a double lumen tube, one-lung ventilation, fem-fem bypass, and excision of the mass via left upper lobe lobectomy.

CONCLUSIONS
There are special anesthetic concerns regarding a chest mass involving both pulmonic and cardiac structures. These include sequence of the operation, one-lung ventilation, and use of the cardiac-pulmonary bypass machine.
Minding the Gap: A Comparison of the Albumin-Lactate-Phosphate Corrected Anion Gap (ALPCAG) to the Strong Ion Gap (SIG)

OBJECTIVE
We sought to determine if the albumin-and-lactate-corrected anion gap (ALCAG) or the albumin-lactate-phosphate corrected anion gap (ALPCAG) could more easily approximate the strong ion gap (SIG), without the cumbersome calculation required for the SIG.

METHODS
We screened all patients admitted to the ICU of George Washington University over a 12-month period for those who had a simultaneously drawn electrolyte panel, albumin, mineral panel and blood gas with lactate. We then calculated AG, albumin corrected anion gap (ACAG), ALCAG, ALPCAG and the SIG. Demographic and relevant clinical data were also collected. These values were tested by Pearson correlation and Bland-Altman assessment.

RESULTS
199 consecutive patients met the inclusion/exclusion criteria. The mean AG, ACAG, ALCAG, ALPCAG, and SIG were 7.3 ± 5.4, 12.1 ± 5.2, 13.6 ± 4.2, 7.5 ± 4.3, and 7.2 ± 3.7, respectively. ALPCAG and ALCAG were highly correlated with the SIG (0.831, p < 0.001 and 0.863, p < 0.001 respectively), and outperformed the AG, and ACAG (0.68, 0.69, respectively) with respect to correlation to the SIG. In Bland-Altman analysis, the ALPCAG more closely approximated the SIG with an ALPCAG-SIG difference of 1.4 ± 1.1 mmol/L.

CONCLUSIONS
The ALPCAG more accurately reflected the true value of the SIG. Since the ALPCAG is easily calculated, the ALPCAG can be used to make a primary assessment of the SIG with fewer variables, and without the need for a programmable calculator or blood gas. If the ALPCAG is abnormal, a formal calculation of the SIG should be undertaken in order to completely assess the acid-base status of a patient.
Pedestrian versus motor vehicle accidents occur commonly in urban settings causing significant morbidity and mortality rates. The purpose of this study was to evaluate and compare the injury profiles and related health costs associated with pedestrian struck accidents treated at a major metropolitan hospital during two 4 year time periods. A review of Department of Motor Vehicle data indicated that sport utility vehicle (SUV) registration in New York City increased by 47% between the two observation periods. We hypothesized that this increased utilization of SUV’s would lead to a higher incidence of severe lower extremity injuries and to higher overall injury severity scores.
School of Medicine and Health Sciences

Corneal Wound Healing Following Corneal Epithelia and Basement Membrane Ablation and the Post-Surgery Application of Helium Cold Plasma Therapy

Background

Cold plasma laser (ionized helium gas) has recently been shown to have an inhibitory influence on the proliferation and migration of fibroblasts in response to tissue injury. In recent years keratorefractive surgeries (laser subepithelial keratomileusis (LASEK), laser in situ keratomileusis (LASIK), and photorefractive keratectomy (PRK)), to adjust corneal shape and therefore refraction, have become very common. These surgeries often involve corneal epithelia ablation and disruption of the corneal stroma. In response to injury in the cornea the body tries to repair itself as stromal cells proliferate and migrate to the injured tissue. In some instances healing occurs with excess fibrosis and visual acuity suffers as a result.

Purpose

These studies examined fibroblast proliferation and corneal reepithelialization rates in rabbits treated with helium cold plasma therapy following corneal ablation.

Methods

Rabbits were randomly put into one of five groups, A, B, C, D, or E. Rabbits in groups A (n=3), B (n=3), C (n=2), and D (n=2) underwent surgery to create a centrally located, 6mm wide, 0.5mm deep corneal ablation in the right eye. Following surgery, rabbits in groups A and C underwent 180 seconds of helium cold plasma application over the scraped cornea. Those rabbits in group B and D did not receive cold plasma application following surgery. Animals in group E (n=2) did not undergo surgery but did receive cold plasma therapy in the right eye. The eyes were monitored for reepithelialization and healing using fluorescein staining and slit lamp examination. Approximately 24 hours after surgery the corneas of rabbits in groups C and D were harvested. On the 20th day following surgery the corneas of rabbits in groups A, B, and E were likewise harvested.

Results

Clinical evaluation of corneal reepithelialization on postoperative day one showed that rabbits receiving cold plasma had an average epithelial defect of 9.25 mm² while rabbits without cold plasma had an average epithelial defect of 12.05 mm², a difference of 30%. The harvested corneas have not yet been evaluated histologically for fibroblast and cell marker evaluation and tests for statistical significance have not yet been undertaken.

Conclusions

The results of these studies have not yet been thoroughly evaluated. However, based on clinical evaluation alone, the corneas of rabbits treated with cold plasma therapy following surgery heal at a faster rate than do the rabbits receiving no postoperative cold plasma therapy.
CHromatin is a dynamic complex of DNA and protein that regulates the flow of information from genome to end product. The efficient recognition and faithful repair of DNA damage, particularly double-strand damage, is essential for genome stability and cellular homeostasis. Imperfect repair of DNA double-strand breaks (DSBs) can lead to oncogenesis. The efficient repair of DSBs relies in part on the rapid formation of foci of phosphorylated histone H2AX (γH2AX) at each break site, and the subsequent recruitment of repair factors. These foci can be visualized with appropriate antibodies, enabling low levels of DSB damage to be measured in samples obtained from patients. Such measurements are proving useful to optimize treatments involving ionizing radiation, to assay in vivo the efficiency of various drugs to induce DNA damage, and to help diagnose patients with a variety of syndromes involving elevated levels of phosphorylated histone H2AX. We will survey the state of the art of utilizing phosphorylated H2AX in clinical settings. We will also discuss possibilities with other histone post-translational modifications. The ability to measure in vivo the responses of individual patients to particular drugs and/or radiation may help optimize treatments and improve patient care.
Video Capsule Endoscopy in the Emergency Department: A Novel Approach to Diagnosing Acute Upper Gastrointestinal Hemorrhage

BACKGROUND
Video Capsule Endoscopy (VCE) is a novel method to diagnose an Acute Upper Gastrointestinal Hemorrhage (AUGIH). Potential advantages include the ability to be performed 24 hours per day without sedation and to be interpreted at the bedside by the ED physician.

OBJECTIVES
Our objectives were to demonstrate (1) ED patient tolerance for VCE (2) the agreement of VCE interpretation between ED and GI physicians for detection of fresh blood and (3) the ability of VCE to detect active bleeding compared to subsequent upper endoscopy (EGD) and/or patient follow-up.

METHODS
This study was conducted over a 6-month period at a single urban academic ED. Investigators performed a VCE (Pillcam Eso2, Given Imaging) on subjects identified by the ED staff to have suspected AUGIH (melena, hematemesis or coffee-ground emesis). Following the VCE, subjects completed a short survey regarding procedure tolerance. Approximately 30 minutes of video were recorded per subject and reviewed by 4 blinded physicians (2 ED physicians with no prior endoscopy training and 2 GI physicians experienced in VCE.) Subjects were followed for clinical outcomes and EGD results.

RESULTS
Twenty-five subjects (mean age 52 years old, 13 female) who described bloody emesis, coffee-ground emesis or melena in the past 24 hours were enrolled. No eligible subjects declined and 96% stated the VCE was well tolerated. No subjects suffered any complications related to the VCE. Between the two GI physicians, there was good agreement on the presence of fresh blood (k=0.84). Compared to the GI physicians’ interpretation, each of the two ED physicians demonstrated good agreement regarding the presence of fresh blood (k=0.83 and k=0.90). The presence or absence of fresh blood on VCE showed a sensitivity of 83%, specificity of 84%, PPV of 0.63 and NPV of 0.94 compared to the gold standard of active bleeding on EGD within 24 hours (20 subjects) or patient follow-up (5 subjects).

CONCLUSION
VCE was well tolerated in ED patients with suspected AUGIH. ED physicians were able to interpret the presence of fresh blood with good agreement with experienced GI physicians. Finally, VCE was accurate in comparison to the gold standard of EGD or patient follow-up for detection of active bleeding.
Comparison of clinical outcomes following Interspinous Process Distractor (X-STOP) Implantation or Interlaminar Lumbar Instrumented Fusion (ILIF) for lumbar spinal stenosis

BACKGROUND
Indirect lumbar decompression for neurogenic claudication has been previously described as a safe and viable technique. Although there are several reports describing the clinical success of interspinous distracting devices, there is a paucity of literature on a new technique using an interlaminar allograft. The objective of this study was to determine the differences in validated clinical outcomes following indirect lumbar decompression using an interspinous device or an interlaminar allograft combined with fusion.

METHODS
Sixty-four patients were followed between 2008 and 2011 after undergoing the X-STOPTM or ILIFTM (Interlaminar Lumbar Instrumented Fusion) procedure. Validated clinical outcomes including Oswestry Disability Index, Zurich Claudication Questionnaire, SF-36 and Visual Analog Scale were administered to patients pre-operatively, at 6 weeks, 6 months and 1 year post-operatively. Baseline characteristics and post-operative complications were recorded.

RESULTS
Six patients in the X-STOP group and 2 patients in the ILIF group were excluded from the final analysis, leaving a total of 28 patients in the ILIF group and 28 in the X-STOP group. Baseline clinical scores were similar and both groups had significant improvement in scores during all post-operative time points. Overall, 15/28 (53.6%) patients in the ILIF group and 13/28 (46.4%) patients in the X-STOP group were considered a “clinical success” based on pre-defined ZCQ criteria.

CONCLUSION
Indirect decompressive techniques for neurogenic claudication offer equivalent clinical outcomes when compared to a novel technique using interlaminar allografts. The addition of direct decompression with a laminotomy and interlaminar fusion does not appear to yield significant clinical benefits at least in the short to mid-term follow-up periods. Longer follow-up is needed to determine whether significant clinical differences will develop.
A 60 year old woman with a history of diabetes presented to primary care clinic with right hand pain. The patient is a legal secretary. Her symptoms started six months ago after a blood draw was taken from the ulnar aspect of her right wrist. Since then, she noted severe pain with associated weakness and diminished dexterity. On physical exam, her neck revealed full range of motion and a non-tender cervical spine. She had 2+ radial and ulnar pulses bilaterally and her wrist exam showed no deformity, full range of motion, and no strength deficits. She had severe atrophy of the first dorsal interosseous muscle and the hypothenar with loss of abduction of her fifth digit (Waternberg's sign). Tinel's sign was positive distal to Guyon's canal but negative over the ulnar nerve at the elbow. There was reduced sensation and prolonged two-point discrimination along the fifth digit. These findings were consistent with ulnar nerve palsy.

Work-up included an EMG which confirmed a severe distal ulnar neuropathy. MRI demonstrated an abnormal growth distal and anterior to the styloid process of the ulna. She was referred to orthopaedic surgery and underwent surgical decompression in Guyon’s canal. Pathology revealed mature adipose tissue. Post-operatively, the patient had no improvement in her atrophy, ongoing pain and decreased motor control of the fifth digit.

**DISCUSSION**

Muscle atrophy generally occurs where there is complete, chronic muscle denervation. Diagnosing intrinsic hand muscle atrophy includes both elucidating an etiology and discerning the location of the lesion. Systemic conditions often present bilaterally and include Pancoast syndrome, Hansen's disease, rheumatoid arthritis, amyotrophic lateral sclerosis and poliomyelitis. Unilateral findings may be due to chronic repetitive trauma, fractures in the wrist, thrombosis, aneurysms, or masses like lipomas, ganglia, or synovial cysts. Sites of possible nerve involvement include anterior horn cells, nerve roots, brachial plexus, peripheral nerves, or the muscle itself. In our patient, severe ulnar neuropathy was secondary to entrapment of the nerve at the wrist by a lipoma and was likely exacerbated by chronic repetitive movements with typing. Indications for surgery in ulnar nerve entrapment are lack of improvement in symptoms 2 months after attempts at conservative therapy, progressive palsy/paralysis or clinical evidence of a long-standing lesion such as muscle wasting. Post-operative prognosis is affected by duration of nerve entrapment and severity of weakness. In chronic cases, improvement may be limited but progression of damage may be halted.
Do Patients Want Spiritual Inquiry in the Emergency Department?

BACKGROUND

Spirituality is associated with improved patient outcomes and quality of life. Recently developed are national consensus derived models of spiritual care for the seriously ill, including the need to identify spiritual distress.

OBJECTIVES

We investigated whether ED patients want inquiry about their spirituality or religious beliefs, which health care provider should inquire and under what circumstances, reasons why they want their provider to know their beliefs, and what they want their provider to do with this information.

METHODS

Setting: two urban ED’s with a single affiliated EM residency, totaling over 100,000 patient visits/year. Design: Cross sectional survey. Trained research assistants asked a convenience sample of adult, non-critically ill, English speaking ED patients if they would participate in a study on spirituality. Written surveys collected demographic information, health survey questions, patients’ rating of scenarios when spiritual screening was desired, reasons for dialogue, and patient expectation of how the emergency physician would use this information.

RESULTS

1377 patients completed questionnaires. Among the last 200 patients approached the response rate was 55% (response rate not initially collected). 57.9% were female and 51.1% were Black (34.3% White, 4.6% Hispanic, 3.9% Asian) 72.2% had a current religious affiliation. Overall, 59% of subjects wanted the emergency physician to ask about spiritual beliefs at least some of the time. 85% of patients wanted spiritual inquiry by nurses or physician assistants. Scenarios most selected by subjects for spiritual dialogue were: severe illness with possible death (81.9%), advanced directive issues (72.4%), and severe illness or death in a family member (79.4%). Subjects desired less spiritual inquiry if they were seen for laceration repair (21.9%) or ankle sprain (19.2%). The most frequent reasons for spiritual dialogue with an emergency physician included the desire for patient-physician understanding and the wish for compassion or hope from the physician. 70% of respondents expected emergency physicians to be informed about their spiritual beliefs so referral to a chaplain or spiritual advisor could be made.

CONCLUSION

A significant proportion of ED patients would like to have a dialogue with their ED provider about spirituality.

Table 1. Subject preference for spiritual inquiry by emergency physician

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious motor vehicle crash</td>
<td>68.3%</td>
</tr>
<tr>
<td>Victim of sexual abuse</td>
<td>58.9%</td>
</tr>
<tr>
<td>Admission to hospital</td>
<td>56.0%</td>
</tr>
<tr>
<td>Domestic violence</td>
<td>53.8%</td>
</tr>
<tr>
<td>Family member with alcohol or drug use</td>
<td>50.4%</td>
</tr>
<tr>
<td>Chronic pain</td>
<td>46.5%</td>
</tr>
</tbody>
</table>
Neuroimaging of Cerebral Neurosarcoidosis: Atypical Features

OBJECTIVE
Neurosarcoid can present on neuroimaging as separate CNS lesions that can mimic other conditions including inflammatory and neoplastic disorders. We report the MR imaging findings in an adult patient with neurosarcoid with atypical features.

METHODS
We report a case of a 47 year-old man who presented with sinusitis, vision loss and marked hyposmia. On admission, conventional brain MRI scans were obtained including diffusion tensor imaging (DTI), these demonstrated large bilateral frontal lesions. MR images were examined for extent and location of the lesions as well as invasion, destruction or displacement of white matter tracts. MRI scans were compared to other cases of white matter lesions lesions for atypical features (N=9) including cases of neurosarcoidosis, Lymphoma, and Progressive multifocal leukoencephalopathy (PML).

RESULTS
CT and MRI scans revealed large bilateral intra-axial frontal white matter lesions with edema. There was also an enhancing mass at the inferior frontal region involving the cribriform plate, olfactory grooves, superior ethmoid sinuses with associated bony involvement. The inferior frontal lesions, adjacent meninges and sinuses demonstrated strong enhancement. DTI maps showed impairment of frontal white matter tracts, with sparing of juxtacortical u-fibers. This combination of findings indicated an inflammatory process affecting more than one structure and causing cerebritis, meningitis and sinusitis. Histopathology showed granulomatous inflammation consistent with sarcoid. The patient’s symptoms and scans improved following standard therapy. Other comparison cases such as PML and lymphoma differed by their degree of involvement of the u-fibers, edema, meninges, sinuses and bony structures.

CONCLUSION
We report the imaging findings of a case of neurosarcoid with unusual features. Although the imaging findings can mimic other etiologies, the unique pattern of involvement of white matter, u-fibers and sinuses as well as enhancement of the meninges supports neurosarcoid. Careful evaluation of the neuroimaging characteristics is important for accurate diagnosis in the appropriate clinical setting.
Neuroimaging of Epilepsy: Uncommon Presentations

PURPOSE
MR imaging of the brain plays a key role in evaluation of anatomical abnormalities involved in epilepsy, but the absence of characteristic lesions can create difficult diagnostic challenges. Although common causes such as mesial temporal sclerosis are well established, uncommon causes of seizures should also be considered in the evaluation of epilepsy, especially in atypical presentations. This study demonstrates neuroimaging findings that can help to in the evaluation of uncommon presentations of seizures.

MATERIALS AND METHODS
Patients presenting to our Medical Center with epilepsy over the past year were selected (n=33) from a clinical database. Clinical presentation included seizures, headaches and language symptoms. Patients had conventional brain MRI including high-resolution acquisitions, including diffusion tensor imaging and spectroscopy. All patients had complete neurologic and electrophysiologic examinations. MR images were examined for various parameters related to lesion characteristics, and diagnoses were confirmed with either neuropathologic examination or laboratory studies. Patients with mesial temporal sclerosis or head trauma were excluded from the study database.

RESULTS
Pathology included stroke, multiple sclerosis, Alzheimer’s disease, paraneoplastic syndrome, gliomatosis cerebri, HIV, CJD, encephalitis, cysticercosis, gliomas, hamartias, cerebellar lesions, cavernomas and metastases. Differentiating features included involvement of brain areas such as thalami (gliomatosis cerebri), bilateral temporal and hippocampal regions (paraneoplastic), inflammatory signs (Multiple sclerosis, encephalitis, cysticercosis), as well as heterogeneity, enhancement, abnormal metabolites (neoplasms), characteristic pattern and evolution (cavernomas, stroke, seizure edema). DTI was sometimes useful in determining the extent of parenchymal and fiber tract involvement.

CONCLUSIONS
Although a variety of lesions can contribute to epilepsy, including the uncommon causes in the differential may be important for accurate diagnosis and management. Careful evaluation of the relevant neuroimaging characteristics is important to augment diagnostic accuracy in the appropriate clinical setting. Further studies, including DTI, MR spectroscopy and follow-up scans may also be useful for further evaluation.
Neuroimaging of Increased Intracranial Pressure and Papilledema

OBJECTIVE

Papilledema, defined as the swelling of the optic disc, frequently occurs in the setting of increased intracranial pressure and in a variety of medical conditions including pseudotumor cerebri, sinus thrombosis, intracerebral hemorrhage, frontal lobe neoplasms and Chiari malformation. Early recognition of papilledema and elevated intracranial pressure is of paramount importance to ensuring restoration of vision. This study examines neuroimaging findings that may provide greater accuracy in the non-invasive diagnosis of increased intracranial pressure and papilledema.

METHODS

Patients presenting to the George Washington University Medical Center with increased intracranial pressure over the past year were evaluated (n=16). The clinical presentation included classical symptoms of increased intracranial pressure, and lumbar punctures showed elevated CSF pressures. All patients had brain MRI scans and MR venograms (MRV) were also performed. MR images were examined for various parameters related to changes in intracranial pressure, including ventricular size, prominence and tortuosity of optic nerve sheaths, stenosis of venous sinuses, as well as the size of pituitary gland, Meckel’s cave and cavernous sinuses.

RESULTS

Abnormalities involving the orbit included widening of the optic nerve sheath (n= 14), flattening of the posterior sclera and tortuosity of the optic nerve. Protrusion of the optic papilla into the globe (papilledema) was noted in a small subgroup of patients, especially those with significantly elevated intracranial pressure. Additional findings also involved empty sellas (n= 13) and decreased size of the cavernous sinus and Meckel’s cave in all cases. The ventricular system was slightly small in some patients (n= 4), but did not generally show classical slit-like narrowed ventricles. Abnormalities of the venous sinuses were detected in most patients, with diffuse or focal narrowing, which could be seen not only on MRV’s but also on conventional MRI’s.

CONCLUSIONS

Non-invasive imaging of increased intracranial pressure and of the optic nerve is possible using magnetic resonance imaging, with a variety of findings involving the orbit occurring in the setting of papilledema. Increased ICP may lead to papilledema through mechanical and ischemic mechanisms. Newer, advanced MRI techniques, such as functional MRI and diffusion tensor imaging, may prove useful in the future to assess the potential effects of papilledema on retinal and visual pathway integrity.
OBJECTIVE
MR imaging of the brain is essential in the evaluation of stroke, but the occurrence of stroke secondary to uncommon pathology can create difficult diagnostic challenges. Although common causes such as thrombosis are well established, uncommon causes of stroke should also be considered in atypical presentations. This study demonstrates neuroimaging findings that can help to in the evaluation of uncommon presentations of stroke.

MATERIALS AND METHODS
Patients presenting to our Medical Center with stroke over the past year were selected from a clinical database. Clinical presentation included acute sensory/motor dysfunction, headache, cognitive changes and aphasia (n=30). Patients had conventional brain MRI including diffusion tensor imaging. MR images were examined for various parameters including lesion characteristics and the presence of other lesions. All patients had complete neurologic examinations, and patients with common types of strokes due to arteriosclerotic plaque, dissection or emboli were excluded from the study.

RESULTS
Pathology included vasculitis, lupus, arteritis, venous malformations, mitochondrial disorders, microangiopathy, inflammatory diseases and bleeding conditions. Differentiating features included involvement of specific brain regions such as inflammatory signs (lupus, temporal arteritis, drug-induced), temporal regions (herpes), basal ganglia (mitochondrial encephalopathy), thalami (artery of Percheron, sinus occlusion), brainstem nuclei (posterior circulation), multiple lesions on susceptibility scans (cavernomas, microangiopathy). DTI was sometimes useful in determining the extent of parenchymal and fiber tract involvement.

CONCLUSIONS
Although a variety of lesions can contribute to stroke, including uncommon causes in the differential can be important for accurate diagnosis and management. Careful evaluation of the relevant neuroimaging characteristics is necessary to augment diagnostic accuracy in the appropriate clinical setting. Further studies, including DTI and follow-up scans may also be useful for further evaluation.
Neuroimaging of Pilocytic Astrocytoma with Anaplastic Features using Diffusion Tensor Imaging

OBJECTIVE

Pilocytic astrocytomas (PAs) rarely occur in adults, and presentation of a pilocytic astrocytoma with anaplastic features is particularly uncommon. Accurate neuroimaging diagnosis is essential but differentiation with other lesions such as glioblastomas can be difficult. We report the MR imaging findings in an adult patient with pilocytic astrocytomas with anaplastic features.

METHODS

We report a 57 year-old caucasian female with a known 20-year history of a midline cerebellar mass who presented with severe gait ataxia. The patient had conventional brain MRI scans including diffusion tensor imaging (DTI). MRI data was processed to obtain tractography and fractional anisotropy (FA) maps. MR images were examined for extent and location of tumor as well as invasion, destruction or displacement of brain parenchyma and white matter tracts. A comparison case of a cerebellar glioblastoma (GBM) was also examined for the above features.

RESULTS

Conventional MRI scans revealed a 4 cm solid and cystic lesion with lobulated margins in the cerebellar vermis, increasing in size from prior studies. Tractography and FA maps showed mostly displacement rather than invasion of the adjacent cerebellar parenchyma and white matter tracts. The comparison case of a cerebellar GBM demonstrated invasion and destruction of the white matter tracts on DTI. Histopathology showed a largely circumscribed astrocytoma with associated macrocysts, microcalcifications, eosinophilic granular bodies and rare Rosenthal fibers, consistent with a pilocytic astrocytoma. However, focally localized atypical features were also present, including a hypercellular focus with increased mitotic activity and pseudopalisading necrosis, consistent with a pilocytic astrocytoma with anaplastic features.

CONCLUSION

We report the unique imaging findings of a biopsy-proven pilocytic astrocytoma with anaplastic features. MR tractography and FA values demonstrated displacement of adjacent parenchyma, which is more characteristic of PA than GBM. However, in the presence of focal anaplasia, long-term monitoring will be necessary, since PAs with anaplastic features may have a high rate of recurrence.
MEDICAL FACULTY ASSOCIATES

Supernumerary Olfactory Bulbs in Humans

OBJECTIVE
To study olfactory bulb characteristics in normal subjects and in patients with smell loss.

MATERIALS AND METHODS
Magnetic resonance imaging (MRI) studies of anatomical structures in the region of the olfactory bulbs were acquired from a series of 220 subjects referred to our Medical Center for evaluation of several clinical complaints (e.g., headache, possible seizure, TIA, etc.). All patients had a standard MRI brain protocol including high-resolution T2-weighted coronal images. All images were carefully evaluated for olfactory bulb morphology and structural abnormalities in the orbitofrontal cortex, rectus gyrus region, olfactory grooves, hippocampi and temporal lobes.

RESULTS
Supernumerary olfactory bulbs were discovered in 16 patients (7.3%) \(N=16\), age 43±16y (mean±SD), range 6-68y], which included 6 males and 10 females. Bilateral duplication of bulbs was present in 15 patients (94%) with unilateral duplication in one patient (6%). Patients exhibited normal olfactory sulci but widened and flattened olfactory grooves [15 of 16 patients (94%)]. Olfactory bulb size was within normal limits in 10 patients (62%) with mild to moderate asymmetry of bulb size in 6 of 16 patients (38%). Olfactory groove depth was decreased with respect to normal in five patients (31%). Hippocampal malrotations were increased compared to normal in five patients (31%). In the one patient with unilateral bulb duplication, a contralateral left fronto-temporal arachnoid cyst was present. Smell function was known to be impaired in only one of these patients (6%) who had congenital hyposmia.

CONCLUSION
On the basis of these observations, olfactory bulb duplication may be more common than is currently recognized. This is the first report of supernumerary olfactory bulbs. This may have occurred since olfactory bulb anatomy has been difficult to image with prior techniques and olfactory bulb anatomy has not been the focus of neuroradiological attention in the past. Functional studies of olfaction among these patients have not been systematically evaluated, with only one patient among the 16 with a known significant loss of smell. The other patients among the 16 studied had no stated clinical changes related to olfactory function.
Neuroimaging of Diffuse Cerebral Toxoplasmosis: Diagnostic Features

OBJECTIVE
Toxoplasmosis is one of the more common cause of CNS infection in immunocompromised patients and can present as single or multiple brain lesions on neuroimaging. However, the imaging findings can mimic conditions such as neoplasms, ischemic disease and other inflammatory processes, making diagnosis difficult. We report the MR imaging findings in a case involving diffuse toxoplasmosis and investigate its diagnostic features.

METHODS
We report a 40 year-old caucasian female who presented with seizures and a prior history of lymphoma. On admission, conventional brain MRI scans including diffusion tensor imaging were obtained. MR images were examined for extent and location of the lesions as well as invasion, destruction or displacement of brain parenchyma and white matter tracts. Neuroimaging was compared to several other cases (N=9) also involving similar multiple bilateral lesions for the presence of differentiating features, pathology included lymphoma, glioblastoma, neurosarcoaidosis, PML, PRES and trauma.

RESULTS
On admission, conventional brain MRI scans demonstrated multiple diffuse ring-enhancing lesions involving different parts of the brain. The initial MRI scans obtained years earlier showed a small lesion in the left basal ganglia. Neuroimaging findings included decreased signal at the borders of the lesions on T2-weighted scans, restricted diffusion within the lesions, impairment of white matter tracts with no gross involvement of juxtacortical u-fibers on DTI, compatible with infection rather than demyelination or neoplasm. The presence of focal basal ganglia involvement is also suggestive of toxoplasmosis. Other cases involving lymphoma, glioblastoma, trauma also showed multiple lesions but without one or more of the above characteristics.

CONCLUSIONS
We report the imaging findings of a case of diffuse CNS toxoplasmosis. The unique appearance of the brain lesions helps to differentiate toxoplasmosis from other etiologies such as neoplastic, inflammatory and traumatic conditions. Careful evaluation of the relevant neuroimaging characteristics is important for accurate diagnosis of these lesions in the appropriate clinical setting. Further studies, including MR spectroscopy and follow-up scans may also be useful for further evaluation.
Medical Faculty Associates

Neuroimaging of Tumefactive Multiple Sclerosis with Atypical Features

Objective

Multiple Sclerosis often presents as multiple focal periventricular white matter lesions. However, Tumefactive Multiple Sclerosis (TMS) can often present as large enhancing lesions and mimic high-grade neoplasms such as gliomas or lymphoma, abscesses, and stroke. We report the MR imaging findings in an adult patient with TMS and unusual cystic features.

Methods

We report a 45 year-old caucasian male who initially presented with seizures 5 years prior to admission. At that time, MRI showed a small periventricular white matter lesion. On admission, the patient presented again with seizures and changes in mental status. Conventional brain MRI scans were obtained including diffusion tensor imaging (DTI). MR images were examined for extent and location of the lesions as well as invasion, destruction or displacement of brain parenchyma and white matter tracts. Neuroimaging was compared to other cases of TMS (N=5) for the presence of atypical features.

Results

On admission, MRI scans revealed multiple bilateral intra-axial heterogeneously enhancing lesions with marked surrounding edema appearing since the prior study of 5 years ago. The largest lesion involved the left temporal lobe with a large fluid component due to a trapped left temporal horn. This feature was not seen in the other comparison cases of TMS. DTI maps showed destruction and displacement of the adjacent cerebellar parenchyma and white matter tracts, and invasion of juxtacortical u-fibers. The combination of findings was suggestive of a demyelinating process rather than glioblastoma or lymphoma. Histopathology showed characteristic features of demyelination with foamy macrophages and gliosis.

Conclusion

We report the imaging findings of a biopsy-proven case of tumefactive Multiple Sclerosis with atypical features. The presence of a trapped and enlarged temporal horn is very unusual and probably due to ependymal adhesions. Although multiple large enhancing lesions were seen on neuroimaging, suggestive of neoplastic, infectious or ischemic processes, there was evidence of periventricular with white matter involvement. Tumefactive MS should be considered in the presence of periventricular lesions, despite their unusual configurations or possible atypical features.
OBJECTIVES
Diagnose and treat photosensitivity reactions and identify common medications that may cause photosensitivity.

CASE
WF is a 67 year old African American gentleman with diabetes, hypertension, dyslipidemia and prostate cancer who presented to the general internal medicine clinic with a rash over his face and neck of three months duration. He described his skin as darkening, scaling and thickening since August. He denied using any new cosmetic or topical products, any new ingestions, use of new soaps or detergents, changes to his medications, or any previous rashes. The patient reported regular sun exposure of the face during twice monthly golf games. He denied personal or family history of lupus or other autoimmune or photosensitive diseases. His medications included atenolol, nifedipine, hydrochlorothiazide, lisinopril, aspirin and simvastatin. He had no known drug allergies. Physical exam was remarkable only for violaceous, scaly hyperkeratotic plaques over the face and neck with notable sparing of the post-auricular and peri-orbital areas as well as directly under the chin. Punch biopsy was performed and revealed a spongiform (eczematous) dermatitis or hypersensitivity dermatitis. He was referred to a dermatologist, who diagnosed photoallergy, most likely due to hydrochlorothiazide. He was treated with desonide 0.5% cream twice daily for three weeks and advised to use mild soap and sunblock with SPF 30 or higher with good effect. Hydrochlorothiazide was discontinued. The rash responded well to treatment.

DISCUSSION
Photosensitivity consists of phototoxicity and photoallergy. It can be caused by either topical or systemic agents. Phototoxicity is an immediate reaction that presents after sufficient UVA exposure and manifests hours later as an exaggerated sunburn. Histology shows an acute inflammatory pattern. The exact mechanism of phototoxicity depends on the inciting molecule, but a common trend is the radicalization of an elemental chlorine atom. In contrast, photoallergy is a far less common, type IV delayed, immune-mediated hypersensitivity reaction that that seems to be T-cell mediated. Photoallergy usually presents as a papulovesicular or eczematous rash that typically appears on sun exposed areas days to weeks after sun exposure. Biopsy reveals a spongiform dermatitis pattern. The most commonly associated medications are diuretics, nonsteroidals, antimicrobials, and antipsychotics. The investigation of photosensitivity reactions should include a detailed exposure history, skin biopsy and photopatch testing. Treatment includes withdrawal of the inciting agent, regular and consistent use of sunblock with SPF of at least 30, and consideration of short-term topical steroids.
The Influence Of Ophthalmology Resident Surgical Simulator Training On Post-surgical Outcomes In Cataract Surgery

PURPOSE
To determine if ophthalmology surgical simulator use during ophthalmology residency training improves patient post-operative outcome in cataract surgery.

METHODS
29 residents were divided into simulator (N=13) and non-simulator (N=16) groups based on the use of the ophthalmology surgical simulator during their residency training. 158 cataract surgeries with residents as primary surgeons were retrospectively reviewed, 81 in the surgical simulator group, and 77 in the non-simulator group. Post-operative visual acuity, corneal edema, anterior chamber inflammation, and intraocular pressure were recorded. Each parameter was recorded on post-operative day 1, post-operative week 1, and post-operative month 1. Patients’ final best corrected visual acuity was also recorded. The visual acuity was calculated using the logMAR chart. Results of the two resident groups were compared using two-tailed T-tests.

RESULTS
Mean post-operative visual acuity was found to be 0.53 (20/68), 0.42 (20/53), and 0.19 (20/31) at post-operative day 1, post-operative week 1, and final best corrected visual acuity, respectively, for the simulator group. For the non-simulator group, the same findings were 0.62 (20/83), 0.52 (20/66), and 0.20 (20/32) respectively. In the simulator group, the mean post-operative corneal edema was 0.73, 0.33, and 0.04 at POD#1, POW#1, and POM#1 respectively. For the non-simulator group, the values were 0.74, 0.32, and 0.06. The mean post-operative anterior chamber inflammation was 1.56, 0.63, and 0.22 in the simulator group on POD#1, POW#1, and POM#1. For the non-simulator group, the values were 1.49, 0.73, and 0.25 respectively. The mean post-operative intraocular pressure on POD#1, POW#1, and POM#1 were 18.64, 15.11, and 14.11 respectively for the simulator group. The same values for the non-simulator group were 20.53, 13.96, and 15.11. Two-tailed T-tests did not reveal a significant difference between the two groups on all parameters (p>0.05).

CONCLUSIONS
Residents who trained using the ophthalmology surgical simulator had similar patient post-operative outcomes as residents who did not in the following parameters: best corrected visual acuity, corneal edema, anterior chamber inflammation, and intraocular pressure. This study provides evidence that use of a surgical simulator during residency training does not change patient post-operative course in cataract surgery.
Prevalence of Helicobacter Pylori Infection in Emergency Department Patients With Upper Abdominal Pain

BACKGROUND
In emergency department (ED) patients with upper abdominal pain, management includes ruling out serious diseases and providing symptomatic relief. One of the major causes of upper abdominal pain is an ulcer caused by Helicobacter pylori (H. pylori), which can be treated and cured with antibiotics.

OBJECTIVES
We sought to estimate the prevalence of H. pylori infection in symptomatic patients using a convenience sample at a single urban academic ED and demonstrate the feasibility of testing in the ED.

METHODS
We prospectively enrolled patients with a chief complaint of pain or discomfort in the upper abdomen at a single academic urban ED. Enrolled subjects were tested for H. pylori using a rapid point of care 13C Urea Breath Test (UBT) [Exalenz Bioscience]. We compared patient characteristics between those who tested positive versus negative for the disease.

RESULTS
150 patients were screened based on chief complaint and 83 subjects were enrolled over a four month period. Among the enrolled subjects, 26.5% (95% CI: 17.0% to 36.0%) tested positive for H. pylori. Non-whites were more likely to test positive for H. Pylori than whites (22/66 (33%) v. 0/17 (0%), 95% CI (8%, 46%). No subjects reported any side effects from the testing.

CONCLUSION
In our ED, H. pylori infection was present in 1 in 4 patients with epigastric pain and testing with a UBT appeared feasible. While not a primary outcome, the risk of infection was higher in patients with non-white race as compared to those with white race. Further study is needed to determine the prevalence of H. pylori in other EDs, its cost-effectiveness in this setting, and which patients have concurrent gastrointestinal pathology such as ulcer, gastric neoplasm or gastritis.

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Design of a Mesenchymal Stem Cell Based Electrospun Fibrous Cartilage Substitute with Biomimetic Nanostructure and Improved Mechanical Property

Articular cartilage repair and regeneration continue to be largely intractable due to the poor regenerative properties of this tissue. Consequently, once injured, cartilage is much more difficult to self-heal. Although traditional methods like autografts and allografts have been clinically employed to treat articular cartilage lesions, there still exist many shortcomings associated with these therapies such as insufficient donor cartilages and donor site morbidity. Therefore, the objective of this project is to design a biomimetic stem cell based nanofibrous construct through an electrospinning technique for cartilage regeneration. Electrospinning is a powerful nano/micro fabrication technique to design various biocompatible tissue engineered scaffold with tunable characteristics such as porosity, fiber diameters, mechanical properties.

In this study, we will seek to explore the effects of varying physical and mechanical properties of electrospun nanofibrous polymer scaffolds on human bone marrow derived mesenchymal stem cell (MSCs) functions. Specially, a series of biocompatible poly(L-lactic acid) (PLLA) scaffolds with different fiber diameters were created by varying working conditions during electrospinning. The morphologies electrospun fibrous scaffolds were characterized by scanning electron microscopy and fluorescence microscopy. Furthermore, the optimized PLLA fibrous dimension for MSC attachment was determined via an in vitro MSCs adhesion study. Then, scaffolds will be co-electrospun with the optimized fibers as a constant parameter, but with varying concentrations of multi-walled carbon nanotubes (MWCNTs) in the polymer solution. The goal of adding MWCNTs to the PLLA scaffold is to create a biomimetic nano surface roughness and change the mechanical properties of the fibers, and to draw a correlation between MSC functions and the mechanical properties of tissue engineered scaffolds. Mechanical testing, MSC proliferation and differentiation will be evaluated and correlated on these novel electrospun nanofibrous scaffolds for improving cartilage regeneration.
Image Fusion and Visualization for Surgical Applications

BACKGROUND
Medical procedures require high levels of precision and acquired skills. With the introduction of volumetric data acquisition modalities, the amount of information available to the medical practitioners has grown exponentially, but the usage of this information is still dependent on the domain knowledge of the physician and their ability to mentally combine and analyze multiple sources of information.

Image-guided surgery aims to help this process by fusing different modalities and visualizing those in a fashion that would give as much information to the physician while removing unnecessary clutter and avoiding information overload. Our research focuses on applying state-of-the-art visualization and interaction methods to improve the success rate and accuracy of surgical procedures.

METHODS
We developed novel visualization methods to display color information from 2D photographs and multiple volumetric medical imaging modalities such as CT and MRI scans. Our image fusion approach merges two registered image modalities (2D and 3D) into a single data set where the correlation of information can be visualized. Photographs and video frames with 3D patient data can be visualized interactively and volumetrically after this fusion process.

Another aspect of visualizing multiple medical modalities is the difficulty of visualizing 3D medical datasets on a 2D screen because of the loss of information due to projection. Transfer functions are used to display relevant parts of the datasets by assigning distinguishable color and opacity values to desired range of intensity values. However, these are applied to the whole dataset and do not take into spatial relationships of anatomical structures. We developed novel visualization methods that enable the user to perform real-time exploration and editing of local regions of multiple volumetric datasets, thereby visualizing the relationships between these multiple datasets.

RESULTS
The proposed methods and visualizing volumetric datasets in general require significant amount of computational resources. We implemented our methods using the features of modern graphics processing units (GPUs), and achieved satisfactory visual quality while maintaining real-time rendering speeds. Novel interaction methods using gestures were also incorporated into the system that can overcome challenges of traditional tactile techniques such as sterilization.

CONCLUSION
We propose and implement novel interactive visualization techniques for multimodal image fusion and visualization. The results presented show we can achieve real-time rendering performance using commodity hardware, and produce visually pleasing and informative visualizations that can improve the surgeons’ understanding of relationship between multiple datasets that are traditionally displayed separately.
Accuracy of the O-Arm for Assessment of Pedicle Screw Position in a Pediatric Porcine Model at A Range of Radiation Doses

The objective of our study is to determine the accuracy of intraoperative O-arm images versus conventional computed tomography (CT) and open dissection in determining pedicle screw position in a pediatric spine model. The current standard of care for severe scoliosis is posterior spinal fusion with pedicle screws that provide rigid fixation to the bony anatomy and long spinal rods to provide structure and internal bracing as well as to achieve a correction of a deformed spine. The modern instrumentation technique for correction of severe scoliosis involves use of intra-operative imaging for pedicle screw placement. The most recent advance is an intra-operative computed tomography (CT) scanner known as the O-arm which can be used for both navigation and assessing accuracy of pedicle screw placement. To test the accuracy of the O-arm, pedicle screws will be inserted bilaterally on immature porcine specimens over the entire thoracolumbar spine. After screw placement, each specimen will be scanned by the O-arm four times under four different doses (adult, adolescent, pediatric, infant) and a portable CT scanner. Each porcine spine will then be dissected as the gold standard for determining exact screw placement. The O-arm and CT results will be presented to a group of experienced orthopaedic surgeons who will rate the pedicle screw placement based on grading criteria. Their ratings will be compared to the gold standard and evaluated for correctness as well as differences between scans at different radiological doses. This project is currently in development.
Case report: The management of emergence delirium in an obese patient with obstructive sleep apnea

Emergence delirium (ED) is characterized by confusion, agitation, paranoia, uncooperativity, and often excitement in the post operative period that occurs in 3-5% of adults. This case report highlights the challenges of the management of ED in an obese patient with the complicating factor of Obstructive Sleep Apnea (OSA). OSA is a frequently seen comorbidity in surgical patients and can result in a complicated post operative course. The treatment of emergence delirium in obese adult patients with OSA is not well characterized and proves to be difficult. Challenges included balancing the need to sedate for the safety of the patient and the healthcare staff with the concern for decreasing his pharyngeal tone and worsening his OSA. While there are no guidelines for the management of this situation in the adult population, there is evidence from the pediatric population as to the benefit of Dexmedetomidine, which proved useful in this situation as well.
Can Patients With A History of Urolithiasis Accurately Self-Diagnose Recurrent Episodes of Renal Colic?

INTRODUCTION

Calculus of the urinary tract is the cause of almost 2 million visits to U.S. emergency departments (EDs) each year. Patients often experience episodes of recurrent pain due to urolithiasis and may undergo abdominal CT scans as part of the evaluation. It is unknown if patients can accurately self-identify recurrent episodes of renal colic.

OBJECTIVES

Can patients with a history of urolithiasis self-identify a recurrent episode of renal colic during an ED visit with high accuracy?

IMPORTANCE

If patients can reliably self-diagnose a recurrent episode of renal colic, physicians may justifiably reduce the number of abdominal CTs ordered to aid diagnosis.

METHODS

We have designed a retrospective chart review of approximately 500 ED patients identified by chief complaint of “kidney stone.” Inclusion criteria is age greater than 18, a chief complaint described by patient as “kidney stone” and a past history of urolithiasis. We analyzed charts for final diagnosis of urolithiasis or related terms.

RESULTS

Patients can identify recurrent renal colic with accuracy. (TBD)

DISCUSSION

Patients with history of urolithiasis can accurately self-diagnose a recurrent episode of renal colic. These findings suggest that CT scans may not be needed for diagnosis in most ED patients with recurrent symptoms. Future studies are needed to determine which patients with renal colic most benefit from CT scans.
EDUCATION/HEALTH SERVICES

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Cultural Adaptations of the Diabetes Prevention Program for South Asian Americans

OBJECTIVE

There are approximately 2.7 million South Asians currently living in the United States, and census reports indicate Asian Indians are the fastest growing minority group. Individuals from South Asia are more likely to develop type 2 diabetes, to be diagnosed at a younger age, and to experience more disease related complications than the general population. Estimates of prevalence indicate 29% of Asian Indians have T2DM and 37% have pre-diabetes. Given the disproportionate burden of type 2 diabetes among the South Asian American population, a valid, culturally appropriate diabetes intervention is needed to prevent the onset of disease. This project is a part of a larger diabetes prevention pilot project (the Diabetes Prevention Study) that will conduct both quantitative and qualitative research to examine behavioral risk factors for developing type 2 diabetes among South Asian American families in the Washington, DC region.

METHODS

This study will use both quantitative and qualitative methods to obtain the complex evidence needed to inform adaptation of the Diabetes Prevention Program for South Asian Americans. Phase 1 will gather quantitative data through a self-administered survey to 120 participants and Phase 2 will focus on qualitative data collected during focus groups and one-on-one interviews with a subsample of 30 participants from the Phase 1 population. The quantitative survey instrument includes questions from the National Health and Nutrition Examination Survey (NHANES), the Michigan Diabetes Center, and previous South Asian studies. The survey includes the following domains: socio-demographics and acculturation, nutrition, physical activity, perceptions of health and diabetes, gestational diabetes, children’s nutrition and physical activity, family activities, health information and technology use, knowledge, and stress. Two qualitative focus groups, one male and one female, will collect in depth information about perception of health risks, dietary behaviors, attitudes about a healthy diet, perceived barriers to a healthy diet, physical activity participation, and attitudes about physical activity. Results: Pending upon completion of qualitative research. Descriptive and bivariate analyses will be conducted using SPSS to assess relationships between sociodemographics, acculturation, perceptions of diabetes, and physical activity/nutrition. Qualitative analysis will be conducted using NVivo.

CONCLUSIONS

Pending upon completion of qualitative research. The results obtained from this study will be used to facilitate the planning of a diabetes prevention program that includes dietary and physical activity components for South Asian Americans. The results will ensure that the program materials, content, and setting are culturally salient to promote behavior change.
With the proliferation of smartphones, mobile phones are being used in novel ways to promote smoking cessation. This study set out to examine the content of smoking cessation, smartphone applications (apps) in the iPhone App Store that were commercially available in January 2012. This study updates the previous analysis in June 2009. Each app in the current sample was coded for its (1) approach to smoking cessation and (2) adherence to the U.S. Public Health Service’s 2008 Clinical Practice Guidelines for Treating Tobacco Use and Dependence. Where available, each app was also coded for its (3) frequency of downloads. Preliminary results indicate that the quality of currently available smartphone apps have improved since the earlier analysis from 2009.
SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

The Forgotten Youth: Facilitating dialogue about love, sex, and relationships to prevent teen pregnancy for adolescents in the DC juvenile justice system

BACKGROUND

In 2009, there were 59.1 pregnancies per 1,000 girls aged 15 – 19 years in the District of Columbia. In order to exert a greater impact on the teen pregnancy rate in DC, it is important to target those teen boys and girls who have multiple risk factors such as being in foster care, being truant, or on probation for other offenses.

OBJECTIVE

In collaboration with the Superior Court of the District of Columbia Social Services Division of the Family Court, the DC Campaign to Prevent Teen Pregnancy have proposed a training series for the juvenile justice personnel on how to communicate with the teens on probation they serve about love, sex, and relationships. This project will examine staff needs with respect to communicating with teens about high risk sexual behavior, in an effort to tailor a two-day program.

METHODS

A sample of 150 adults working as Family Court judges, probation officers, social workers in the child welfare system, and juvenile justice personnel from the Department of Youth Rehabilitation Services will be recruited. Prior to attending the trainings, the personnel will be required to complete an on-line survey that will address knowledge, attitudes, and barriers surrounding the dissemination of sexual education and contraception information from the personnel to the teens they serve. In addition to the surveys, a total of eight (8) one-hour interviews will be conducted with 8 personnel (2 from each job category) prior to their participation in the training.

RESULTS

Results TBD. Descriptive quantitative analyses using SPSS 19.0 will be conducted to assess knowledge, skills, barriers, and attitudes among the study participants in regards to sexual education and contraception. Qualitative interview data will be analyzed with NVivo.

CONCLUSION

The findings from this needs assessment will highlight knowledge, barriers, and attitudes of the personnel who work with at risk teens in the juvenile justice system and, as a result, what are the best approaches for communicating information surrounding sex, sexuality, and contraception. Recommendations will be made to improve and tailor the “Love, Sex, Values, and Relationships” training series; especially for the specific target population of juvenile justice personnel in the Superior Court of the District of Columbia Social Services Division of the Family Court.
This is the first study to assess health-promoting behaviors of PH students using a validated measure.
purpose
Motivation is an important factor in exercise participation. Human behavior and drive to act are influenced by a dynamic composite of internal and external influences. Self-motivation, a person's desire to activate or persist with a particular behavior, includes both intrinsic and extrinsic variables believed to exist along a continuum. In this study we examined the motivation of people with long-time memberships to health clubs to determine if there were differences in motivational factors related to age and sex.

methods
We presented the Exercise Motivation Scale (EMS), a 31 question, 6-point likert scale survey, to 512 health club users via SurveyMonkey. Means of the sums for all sub-categories (motivation facets) were compared among 3 age groups, “young,” “middle,” and “old” and between sexes. Analysis was via 3-way Repeated ANOVA.

results
A significant difference (p<.001) across motivational facets was noted for all age groups combined. Average scores for motivational facets: Amotivation, Ext Regulation, IntrojectedReg, Identified Reg, Integrated Reg, Intrinsic Motiv/Learning, IntrMotiv/Accomplishment, and IntrMotiv/Sensation were 5.4, 7.2, 13.7, 20.5, 14.9, 17.5, and 18.8, respectively. Females trended to slightly higher scores (p<.04) in intrinsic factors; eg. for IM/Learn, 15.4 vs 14 and IM/Sens, 17.6 vs 16.7. No significant differences were found across the age groups; in fact, all age groups exhibited the same trend/pattern in their scores.

conclusion
Understanding motivation for exercise is essential for understanding how to encourage individuals to begin and persist with exercise. The findings of this study suggest there is very little difference in the type of motivation to which individuals of varying age groups and sex are responsive within the setting of health clubs. Therefore, marketing and programming efforts may be best directed toward fostering conditions to promote continued use of facilities/programs. We believe that further study should be directed towards comparing motivational factors of non-exercisers to those of health club members. A better understanding of motivation to exercise would enhance our ability to encourage people in our sedentary society to become physically active.
**BACKGROUND**

The Washington Enrichment and Cultural Arts Network (WE CAN) is a nonprofit organization designed to create a positive and healthy alternative culture that enables underserved youth to reach their educational, artistic, and personal potential to become advocates of hope within their community.

**OBJECTIVES**

The purpose of this project was to assess participant satisfaction and their perceptions of three criteria reflecting the competencies in WE CAN’s youth development curriculum. The following three pillars establish the foundation for community-building, self-efficacy and empowerment through; 1) Safety and Structure, 2) Belonging and Membership, 3) Self-worth and Ability to Contribute.

**METHODS**

Investigators authored a pre-test and post-test evaluation tool. Pre-test surveys were distributed on site four weeks after the start of the program to 20 participants, ages 14-24 yrs. in two rounds. Each participant was given a unique identifier. Follow-up and parental consent forms were completed and collected. Round one was administered on November 19, 2011 and round two on November 30, 2011. Two types of surveys were distributed which included open-ended and Likert Scale (1 strongly disagree to 5 strongly agree) questions. Survey questions were created to best reflect participant satisfaction and feelings toward WE CAN’s youth development curriculum and progress over time within the program.

**RESULTS**

WE CAN pre-test evaluation revealed high levels of feelings related to each of the three core pillars of the program. Questions pertaining to the safety and structure pillar received the highest mean response (4.8), while the ability to contribute pillar (4.6) and the membership and belonging pillars both received slightly lower mean responses (4.5).

**CONCLUSION**

The WE CAN pre-test and post-test evaluation tools address the organization’s focus on the three pillars. The mean responses within each pillar are expected to be higher in the post-test survey, which will be administered in the Spring of 2012. However, results may not be as significant as expected because the pre-test results already indicate high levels of feelings towards the three pillars. This is based on a 90% return rate of WE CAN participants. This statistic reveals opportunities for WE CAN staff to capitalize on performing extensive outreach to new members in order to cultivate immediate positive connections as returning participant responses suggest they have already benefitted from the program. Results from the pre-test survey establish the baseline measurement for WE CAN to chart continued program success moving forward.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Delayed Diagnosis of Acute Cholangitis Proved Deadly: Identifying Cognitive Errors in Diagnostic Process

INTRODUCTION
Despite fever, jaundice, and right upper quadrant (RUQ) pain in this clinical case, defects in cognitive processes delayed the diagnosis of acute cholangitis and contributed to patient death. Cognitive errors commonly cause misdiagnoses through faulty data collection or interpretation, flawed reasoning, and/or incomplete knowledge. Recognizing the defects in cognitive processes that led to diagnostic errors in this case can lead to increased cognitive awareness and reduction in diagnostic error and its associated morbidity and mortality.

CASE
A 76-year-old male with a past medical history of alcohol abuse presented to an outside hospital (OSH) emergency department with abdominal pain. He denied urinary symptoms, but urinalysis revealed a urinary tract infection (UTI) so he was prescribed a two-week course of Nitrofurantoin and Tylenol as needed. Six days later, the patient presented to our emergency department with persistent abdominal pain. On focused questioning, patient endorsed urinary frequency and urge, and since urinalysis was positive for leukocyte esterase, white blood cells, and 4+ bacteria, the emergency department deemed his presentation consistent with urosepsis and called internal medicine for admission. Upon discussion with the patient, he reported persistent RUQ pain for the past 6 days, not relieved by his UTI treatment. The patient denied excessive alcohol use during or prior to his presentation and denied any history of alcohol withdrawal. Physical exam revealed a cachectic male, with scleral icterus and a resting tremor. Abdominal exam showed localized tenderness to palpation in the RUQ, hypoactive bowel sounds, and a negative Murphy’s sign. Laboratory revealed leukocytosis (WBC 11,000) and elevated liver function tests (AST 196, ALT 109, Alkaline Phosphatase 191, Total Bilirubin 5.0, and Direct Bilirubin 3.3). The patient was admitted to internal medicine for treatment of alcoholic hepatitis, alcohol withdrawal, and acute cholecystitis. Two days following admission, the patient became febrile and hypotensive with positive blood cultures that later grew Klebsiella Pneumonia, and required transfer to the medical intensive care unit for suspicion of acute cholangitis. He was transferred back to the floor on day 5 of admission after ERCP was attempted but unsuccessful. The patient was scheduled for MRCP, however despite supportive care and broad spectrum antibiotics, the patient expired after being found lethargic with weak pulses on hospital day 7. Autopsy revealed a distended gallbladder, firmly adherent to the liver bed, with markedly thickened walls and a lumen filled with viscous, purulent material containing innumerable 0.1cm black stones. Histologic sections of the cystic duct and gallbladder showed transmural acute and chronic inflammation consistent with acute cholangitis.

DISCUSSION
This case demonstrates the diagnostic confusion which may occur when clinical decision making is influenced by defects in cognitive processes leading to diagnostic errors. Although RUQ pain, fever, and jaundice that comprise Charcot’s triad, used to diagnose acute cholangitis clinically, were documented during the patient’s presentation, defects in cognitive processes led to delayed diagnosis and treatment. The prior diagnosis of a UTI from the OSH led to tunnel vision in the emergency department and premature closure when other diagnoses that better fit the chief complaint should have been pursued (satisfaction of search). The prior history of alcohol abuse indicating possible alcoholic hepatitis and alcohol withdrawal were elevated to a high level (framing effect) and were used to rationalize the patient’s symptoms of severe suppurative cholangitis. Additionally, confirmation bias (confirming what is expected by selectively accepting or ignoring information) and anchoring (a shortcut in thinking where one does not consider multiple possibilities, but swiftly and strongly chooses a single one) occurred, magnifying the patients lab values that showed a 2:1 ratio between AST and ALT, causing minimization and rationalization of contradictory data (bilirubin of 5.0). Furthermore, subsequent physicians (internist, surgeons, and radiologists) adopted the prevailing misdiagnoses throughout his stay, which all contributed to delays in proper diagnosis and treatment, and subsequent death of our patient that could have potentially been avoided. The majority of patients with acute cholangitis respond to antibiotic therapy with resolution of the biliary tract infection, but urgent endoscopic bile duct drainage is ultimately required to cure the underlying obstruction and nidus for infection. Clinicians should be aware of how to identify and avoid traps in the cognitive processes they routinely use when working up patients in order to avoid diagnostic errors, delays in proper treatment, and associated mortality.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Competency Assessment of Peer Teachers

BACKGROUND
Near peer teaching has long been a stronghold of medical education. In the realm of medical students, peer teaching offers a number of advantages, namely alleviating faculty teaching burden and training young clinicians as future medical educators. This approach to education allows the learner a unique opportunity to be taught by an educator who is close, in training and motivation, to the subject matter. The current literature demonstrates that peer-assisted learning practices produce results comparable to faculty-led training in technical procedures and clinical skills. However, studies have not yet attempted to assess the competency of peer teachers prior to their teaching activities. We designed and implemented a near peer medical student teaching curriculum for bedside ultrasound, and assessed the competency of near peer teachers prior to, during, and after their teaching activities.

METHODS
Fourth year medical students were trained in the point-of-care ultrasound by ultrasound faculty from the department of emergency medicine. Directly prior to and following teaching students completed self-assessment and submitted five ultrasound imaging clips to demonstrate competency. Additionally, first year medical students and standardized patients assessed the instruction by fourth year medical students during the ultrasound instruction session. All assessments were written surveys that had IRB approval.

RESULTS
As compared to pre-sessions survey assessments, the fourth year medical students all reported that they were better able to identify the right upper quadrant anatomy of the abdomen, with most confidence in capturing the liver and least confidence in capturing the portal triad. Additionally, the confidence score for teaching first year medical students how to both identify a normal gallbladder and use the ultrasound machine increased by a full point on the survey scale. Finally, the standardized patients and first year medical students rated fourth year medical student teachers and the entire learning experience on average a 4.5 out of 5.

CONCLUSIONS
Here we demonstrate that fourth year medical students are capable of both learning basic ultrasound maneuvers in a short period of time and subsequently teaching junior medical students how to effectively identify images of the right upper quadrant. Furthermore, the teachers gain confidence and improve their ultrasound ability after teaching this session. Finally, first year medical students reported, and in some groups demonstrated, increased understanding of right upper quadrant anatomy. Ultimately the results of this study will aid in optimizing training of fourth year medical students as medical educators as well as improve current teaching of right upper quadrant anatomy to first year medical students.
EDUCATION/HEALTH SERVICES

SCHOOL OF NURSING
Interdisciplinary Geriatrics Education Using a Palliative Care Framework (GEPaC)

BACKGROUND
Americans are living longer than ever before with an average life expectancy of almost 78 years. With longer life spans and medical advancements for treating illness, older Americans are experiencing greater burden from multiple progressive chronic diseases, including chronic pain, loss of function, and increasing dependence on family and friends. This paradigm shift requires preparing interprofessional healthcare providers to meet the unique needs of older adults for disease management, pain and symptom management, communicating around goals of care, and other palliative care needs, as well as knowledge and skills in geriatrics and gerontology.

METHODS
The George Washington University School of Nursing with funding from Health Resources and Services Administration developed the interdisciplinary Geriatric Education Using a Palliative Care Framework (GEPaC). It will improve care of older adults across the health care continuum, and foster interprofessional education to prepare clinicians to provide more coordinated, continuous health care.

OUTCOMES
GEPaC includes six online modules to educate physicians, nurses, advanced practice nurses, occupational and physical therapists, physician assistants, and other clinicians. The modules are: (1) Geriatric Palliative Care: for integrating the clinical, goals-oriented focus of geriatrics and the holistic, compassion-oriented focus of palliative care; (2) Person and Family-Centered Care: for prioritizing the older adult and family needs, preferences, physical and psychological development, experiences and routines in goal setting and care planning; (3) Interdisciplinary Collaboration: for collaborative strategies and the integration of appropriate healthcare professionals to maintain independence, prevent or relieve suffering, and promote optimum health; (4) Communication: to facilitate effective dialogue and informed decision-making among older adults, families and other providers; (5) Quality of Life: to focus on supporting critical older adult and family issues that impact their health, coping, death and bereavement, taking into account expected patterns and variations of growth and development; (6) Multidimensional Approach to Suffering: for incorporating and managing the physical, psychological, social, and spiritual aspects of suffering. These innovative online learning modules integrate a variety of media, case examples, and interactive activities to engage and motivate learners. The modules can be used individually, together with traditional classroom instruction, or in purely online settings with an Instructor Guide to support educators in effectively integrating the modules with other learning experiences. The poster illustrates the modules, describes the design and development process, and provides access information for educators interested in integrating the online modules into their health professional curriculum.
Residents as Teachers (RAT) Publication: What can Training Programs Learn From the Literature When Starting a New or Refining an Established Curriculum?

BACKGROUND
Teaching residents how to teach is a requirement of the ACGME guidelines 1) to improve the educational interactions between trainees and 2) to make learning most effective and efficient. The importance of formal RAT curricula has been noted in the literature; however, a recent review of RAT curricula revealed that not all residency programs have such a curriculum in place.

OBJECTIVE
The purpose of our study was to review the existing literature for established RAT curricula and assess the curriculum's reproducibility and the type of outcomes evaluated using Kirkpatrick's model of evaluation. We sought to identify explicit curricula that training programs could feasibly adopt.

DESIGN/METHODS
The authors performed a literature review using PubMed, Medline, Scopus, PsycINFO, ERIC, and Embase. Key search words included “residents,” “residents as teachers,” “teaching,” “internship and residency,” and “curriculum.” In addition, a search of MedEdPORTAL was performed using the same key terms. Articles were evaluated based upon the reproducibility of curriculum, assessment tools and the Kirkpatrick assessment levels of each curriculum. Study outcomes were scored using Kirkpatrick's model.

RESULTS
More than 50 articles and MedEdPORTAL resources were deemed appropriate for review. Interventions included workshops, handbooks, teaching electives, lectures, retreats, videos, and online learning modules. Evaluation techniques included resident self-evaluation; questionnaires; learner, mentor, or peer evaluation; observed structured teaching exercise; written knowledge test; and videotaped evaluation. Only four of the studies met the criteria for being fully replicable by including a thorough description of the curriculum/intervention and reproducible outcome measures. Nearly all of the studies utilized Kirkpatrick's levels 1 and 2 evaluation, assessing residents' reactions and learning. However, most studies did not assess residents' change in teaching behavior, levels 3 and 4.

CONCLUSIONS
A literature review on RAT curricula found a paucity of articles that would be easily reproducible for programs to start or improve RAT curriculum within their residency program. It also demonstrated a lack of rigorous outcome measurement for most curricula. The study emphasizes the need for a national resource clearinghouse to assist programs development and better outcomes evaluation.
Background

Narrative medicine is the ability to acknowledge, absorb, interpret, and act on the stories and plights of others, utilizing such tools as storytelling, reflective writing, close reading and representation through art. A pilot narrative medicine curriculum for third-year medicine clerkship students involved eliciting stories from patients about their illness experiences during their hospitalization using narrative medicine techniques. We were interested in knowing the content of what patients shared in this narrative medicine format.

Methods

The pilot narrative medicine curriculum occurred between July 2011 and November 2011. The curriculum involved an introductory session on narrative medicine, including a practice session on eliciting and attentively listening to an open-ended story. Students then used this technique on a patient of their choosing and then reflected upon this experience through a facilitated small-group discussion and/or reflective writing. Eighteen patient stories, as told to and written by students, were qualitatively analyzed for themes. Two authors (JK, KC) read all stories in their entirety and then independently performed line by line coding to develop themes. Themes were discussed until consensus was reached. Themes were categorized into broader categories, which was peer-reviewed by the other authors (RS, BY). Any discrepancies were resolved through discussion. This study was reviewed by the Washington DC VA Institutional Review Board and determined to be exempt. The subjects participated on a voluntary basis.

Results

Themes within patient illness narratives fell into two broad domains: sources of strength and sources of challenge. Sources of strength included optimism, faith, family relationships, self-transformation and self-reflection, curiosity, humor, and perseverance. Sources of challenge included fear/worry, mistrust in medical care, frustration, confusion about their illness, perceived poor care, and pain.

Conclusions

Eliciting patient storytelling through narrative medicine techniques results in themes not usually captured in traditional history-taking, which is focused on generating a differential diagnosis. Shared stories revealed patients’ emotional reactions to dealing with illness and elucidated both sources of strength and challenge; this has the potential to further student understanding, humanism, and empathy. Future studies should explore the depth of student and patient experiences engaging in the practice of narrative medicine.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Mobile Healthcare: Innovations in Telemedicine

BACKGROUND

Telemedicine is the use of communication technology to deliver healthcare. Mobile health is the use of mobile devices, such as diagnostics, remote monitoring, tracking, medication reminders and many other modalities that provide mobility to healthcare providers and patients.

PROJECT

In June 2011, The George Washington University held its first Summer Institute entitled Mobile Healthcare: Innovations in Telemedicine. The Institute was an intensive weeklong multi-disciplinary course for graduate students and professionals from all backgrounds. The course incorporated aspects of business, medicine, public health, and technology. As a Gill Fellow, I worked with the course coordinator to develop the curriculum and course evaluation tools.

THE COURSE

Participants had the opportunity to listen to and interact with speakers across all functions of telemedicine and mobile health. Highlights included topics such as the mHealth Ecosystem, Federal regulation in Telehealth, Global mHealth, app design and development, and self-tracking. The course began with a broad overview and then strategically examined particular aspects of the space, to help students understand how telemedicine and mobile health can be integrated into their respective fields. A final project in which each team designed a novel mHealth strategy was required. Projects ranged from a mobile app for first responders to track casualties in a disaster to an app designed for new parents to schedule their children's vaccinations.

RESULTS

Feedback from course participants was very positive. In a pre- course survey, 28% of students rated their understanding of telemedicine as "very little" (on a 1 to 5 scale). Post- course, 100% of participants rated their understanding within the range of 3 to 5, with 69% rating a 4.

FUTURE DIRECTIONS

The Summer Institute will be held again this year. In addition, there is an ongoing effort to develop a textbook utilizing this same multidisciplinary approach.
Developing empathy: does a patient shadowing experience improve resident caring?

BACKGROUND

Empathy from anesthesiologists improves patient satisfaction and decreases patient anxiety in the preoperative period. The purpose of this study is to assess improvement in empathy for incoming anesthesiology residents following exposure to an observational experience with perioperative patients. Through this process, we hope to increase empathy, understanding of the process, and eventually improve patient care.

METHODS

The incoming class of 7 anesthesiology residents to The George Washington University Medical Center completed a pre-experience inventory regarding their understanding of the patient perioperative experience and how they perceive patients. Each resident shadowed a patient during the admitting process, the preoperative period, and in the PACU. Residents only observed the interactions and did not participate in the process. Residents later completed a post-experience survey and debriefing session. Questionnaire scoring was analyzed with statistical change in performance from pre- to post-test.

RESULTS

All seven residents completed the pre and post questionnaires. Two felt the process was slow and disorganized, two felt it was rapid and streamlined, and three felt it was average. On average, residents changed their opinions about 2.7 questions with most change in the interpersonal reactivity index. Two residents felt they listened to others less if they were sure they were correct. One resident felt more critical after the intervention, and one felt it was more difficult to convince people to listen. All residents disagreed that they try to imagine what it is like to be the other person before criticizing someone both before and after the intervention. Further statistical analysis is pending.

CONCLUSIONS

Post-intervention, little change in empathy was seen. The personality inventories may be poor measures of empathy or residents may be unchanged by a single intervention. This program requires further assessment and refinement with a larger number of residents.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

LOVE Program: Teaching Teens to Love, Own, Value and Empower Themselves

Teenagers faced with social and economic difficulties often lack the parental support and adult guidance necessary for developing adequate personal health skills. Douglas Kirby, a leader researcher of effective pregnancy prevention programs at ETR Associates has noted: “...Youth may have the knowledge, skills, and ability to get and use contraceptives, but if those youth are not connected to family and school and do not believe that their future is promising and worth protecting, then they may not be highly motivated to avoid teen pregnancy.”

With this theory in mind, I developed the LOVE program to educate teenagers about sexual health, but also to help them learn about and explore their own drives and passions. As such, the LOVE program has focus both on the importance of the ABC’s -- Abstinence, Be faithful, and Contraception -- as well as exploring the requisite motivations for putting these concepts into practice. It was my hope that by encouraging teenagers to discuss these issues with their peers in a supportive environment, they would develop the desire and motivation to protect themselves against pregnancy and STIs.

With the help of the Lazarus Family Scholarship, I was able to implement this program in two distinct settings over a two-year period. The first year, I conducted monthly meetings for inner city, at risk, high school aged girls in Washington, DC to talk about body image, sexual well being, future goals, and healthy living. The second year, I worked with two distinct groups of impoverish adolescents from two different rural communities outside of Cusco, Peru. In each community I held bi-monthly meetings to discuss reproductive health, improving communication and interpersonal relationships, as well as mental health.

Though it is difficult to assess the long-term effectiveness of this program the exit interviews revealed that the teens felt comfortable and confident asking about and discussing difficult and sensitive topics.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Residents’ Perception of the Impact of the 2011 ACGME Duty Hour Standards on Patient Safety and Quality of Care

INTRODUCTION

In July 2011, the Accreditation Council on Graduate Medical Education (ACGME) implemented new duty hour standards for residents, designed to assure patient safety and quality of care in teaching hospitals. We conducted a survey to evaluate residents’ perception of how the 2011 duty hour standards impact patient safety and quality of care.

METHODS

A 16-question survey was administered to all residents at a large tertiary care teaching hospital in Washington, D.C. Using a Likert scale, participants were asked how the 2011 duty hour standards impacted quality of care, continuity of care, patient-physician relationship, medical errors, communication of patient medical information, performance of procedures, and faculty supervision. Additionally, opinions on which specific duty hour standard most impacted patient safety and quality of care were assessed.

RESULTS

The overall response rate was 25.6%, which was comparable across specialties and post-graduate training levels. Ninety-five percent of respondents were aware of the 2011 ACGME duty hour standards. Over 75% of residents believed that the new standards would have no impact on faculty supervision. Residents believed continuity of care (58%) and accuracy of patient information during hand-offs (49%) would be negatively impacted. Respondents identified the 16 duty hour limit for PGY-1 residents as having the largest negative impact on patient safety (73%) and quality of care (82.5%).

DISCUSSION

Residents’ perceptions are important in the development of duty hour regulations. Negative perception of the PGY-1 16 duty hour limit highlights the potential impact of this standard on continuity of care and frequency of hand-offs. Residents did not perceive changes in faculty supervision as impacting patient care, which may reflect a lack of awareness of this important goal. Understanding how residents perceive duty hour regulations is essential to improving patient safety and quality of care, a major goal for the 2011 ACGME duty hour standards.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Evaluating the July Effect on Cesarean Delivery Operative Times and Associated Neonatal Outcomes

OBJECTIVE
To examine if cesarean delivery operative time differs by month performed in an academic year at a university-based residency teaching program, and subsequent neonatal outcomes.

METHODS
This is a retrospective cohort study comparing operative times for cesarean deliveries by OB-GYN residents during July 1-August 31, 2009 and 2010 and April 1-May 31, 2010 and 2011. Primary outcome was cesarean delivery operative time. Secondary outcomes were estimated blood loss, neonatal Apgar scores and neonatal disposition.

RESULTS
From July 1 to August 31, 2009 and 2010 and April 1 to May 31, 2010 and 2011, 130 and 111 cesarean deliveries were performed, respectively, in singleton pregnancies at 37 weeks gestation or greater. Demographic and neonatal parameters were comparable. Cesarean delivery operative time was 11.72 (±5.83) minutes amongst the July to August group and 11.05 (±7.07) minutes within the April to May group (p=0.45). There was no difference in disposition to term nursery versus NICU (p=0.46). Estimated blood loss was significantly lower at the beginning of the academic year, 793.31 mL (±268.27) compared to 845.15 (±275.21) mL (p=0.086).

CONCLUSIONS
The "July Effect" does not appear to affect cesarean delivery operative times in the cohorts studied. This may be due to more direct supervision of the novice resident at the beginning of an academic year. Length of procedure did not correlate to any significant neonatal adverse effects. Additionally, the system for teaching new residents appears successful; as first year residents advanced to primary surgeon throughout the year, patient outcomes remained consistent.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Rapport Building: We Teach It- Do Students Use It?

PURPOSE

Although our clinical skills course teaches first and second year medical students rapport building skills, we do not know how often and how well they implement them with patients during their clinical years. The purpose of this study is to:

1. Determine how often third year medical students utilize rapport-building utterances in a required end-of-third year standardized patient (SP) Objective Structured Clinical Exam (OSCE).

2. Understand the impact of these utterances on SP satisfaction.

METHOD

We created a rapport building coding scheme using seven not-mutually exclusive categories: Empathy, Reassurance, Clarification, Summarizing Question, Summarizing Statement, Positive Talk, and Other. A researcher, who demonstrated inter-rater reliability compared to a faculty expert, rated 133 videos, all depicting the same abdominal pain case. We determined the frequency of student rapport-building utterances and correlated that with SP satisfaction scores.

RESULTS

Of the seven categories, the three most used were: Reassurance (112 students), Empathy (110 students), Clarification (101 students), accounting for 92% of the utterances. Of the 133 students, 70 gave at least one instance of all three types, 51 gave two, while only one student provided none. SP satisfaction correlated positively at a statistically significant level with the total number of student rapport-building utterances \( r = .28 \) (\( p = .001 \)), as well as the specific number of Reassurance \( r = .30 \), \( p = .0005 \) and Clarifying Statements \( r = .18 \), \( p = .04 \).

CONCLUSIONS

In an OSCE almost 100% of the third year medical students used rapport-building communication skills taught in their preclinical years. The total number of rapport-building utterances correlated significantly with patient satisfaction. These results support that students effectively implement the verbal rapport-building skills that we teach them. In the future we intend to examine non-verbal along with verbal rapport building behaviors in both simulated and real patients.
Educating/Health Services

School of Medicine and Health Sciences

Analyzing the Embedded Librarian Service

Since fall 2009, reference librarians at The George Washington University’s Himmelfarb Health Sciences Library have been embedded in online classes through Blackboard within the School of Nursing and School of Medicine and Health Sciences. The authors sought to determine the types of questions asked of the librarian, with the goal of informing future interactions with distance education classes to help develop a standard “protocol” for working with this population of students. Eighty-two questions were categorized and qualitatively analyzed. The findings have prompted librarians to expand their support options and explore tools such as Elluminate Live!, a tool that allows librarians to provide synchronous instruction within the Blackboard environment. Additional information on the evolution of the embedded librarian service and support tools in recent semesters will also be included.

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Does Mission Matter? Searching for Social Accountability in U.S. Medical Schools’ Missions, Student Experiences, and Outcomes

Since Flexner’s report, medical education has been rooted in the scientific method, embracing the tripartite missions of education, research, and patient care. However, predicted healthcare disparities have brought into question whether medical education has been successfully addressing the needs of society. Because of this, schools have been urged to include “social missions” in mission statements.

**Objective**

1) Evaluate mission statements of U.S. allopathic medical schools, categorize/quantify stated priorities emphasizing social mission. 2) Test association between schools’ missions and their graduates’ educational experiences and practice outcomes.

**Design**

Mixed methods study, with dual qualitative review of mission statements of LCME accredited medical schools, reported online or in 2012-13 Medical School Admissions Requirements, published by the Association of American Medical Colleges. Quantitative analyses - descriptive data on stated missions, correlation between mission and medical school experiences and outcomes.

**Setting**

137 U.S. Medical Schools accredited by the Liaison Committee on Medical Education.

**Main/Secondary Outcome Measures**

Number/variety of schools whose missions address societal need (student-body diversity, service to underserved, entry into primary care). Associations between stated social mission and a) matriculating characteristics (% rural, underrepresented minority, SES background, primary care interest), b) medical school experiences (quality of family medicine clerkship, community medicine experience, service to underserved, etc), c) workforce outcomes (% entering primary care, practicing in underserved areas).

**Anticipated Results**

Initial review of missions suggests few schools demonstrate strong emphasis on social mission. It is anticipated that the outcome associations demonstrate the degree to which mission statement reflects commitment to social mission, and workforce diversity that is prepared to meet the needs of society.

**Conclusion**

If mission matters, schools with socially-oriented missions will demonstrate greater likelihood of meeting these objectives. The collection of all schools’ mission statements offers insight into the readiness of our nation’s medical schools to meet societal needs.
Improving Trainee Recognition of Factors that Contribute to Clinical Decompensation of Inpatients: A Review Study

BACKGROUND

In December 2004, the Institute for Healthcare Improvement launched the 100,000 Lives Campaign, a national initiative attempting to save 100,000 lives among patients in hospitals through improvements in safety and effectiveness of healthcare. All of the nation’s 5,759 hospitals were invited to participate and encouraged to follow six hospital interventions. The first of these six interventions was to institute Rapid Response Teams (RRT) within the hospital infrastructure. Since the beginning of this campaign there has been an increase in the number of U.S. Hospitals implementing Rapid Response Teams. These teams are a multidisciplinary group of medical, nursing, and respiratory therapy healthcare providers charged with the evaluation, triage, and treatment of patients with signs of clinical deterioration not treated in the intensive care unit (ICU). Despite the internationally widespread implementation of these teams, robust evidence to support their effectiveness in reducing hospital mortality, preventing unexpected cardiac arrests, unexpected deaths, and unplanned admissions to the ICU is lacking and controversial. The objective of this study was to retrospectively review rapid response team cases at George Washington University Hospital in order to identify within these medical records the frequency and trends of historical and physiological factors that have been hypothesized to predict clinical decompensation of inpatients. Through determining the most statistically significant predictive factors of clinical decompensation, an educational module formulated in order to teach these factors to George Washington University HospitalInternal Medicine residents can be implemented for the end purpose of decreasing hospital mortality and the number of adverse events.

METHODS

Initially a thorough literature review of previously identified predictors of clinical decompensation was performed as well as a review of the effectiveness of rapid response teams on decreasing hospital mortality, unexpected cardiac arrests, unexpected deaths, and unplanned admissions to the ICU. A database consisting of these previously identified predictors was compiled and data extraction from the medical records of 30 rapid response/code blue cases within the past year is currently being done in order to determine whether any of these predictors are statistically reliable in foreshadowing patient deterioration. If certain factors are found to be reliable than analysis of a larger number of rapid response/code blue cases will be performed to better ascertain the predictive strength of these factors.

RESULTS

Data and analysis from the initial 30 cases should be completed by March/April 2012.

CONCLUSIONS

No preliminary conclusions can be made at this time.

REFERENCES

INTRODUCTION

Genetics is a relatively new field in medicine that is not yet taught comprehensively in graduate medical education. Current physicians often do not have the skills necessary for practicing or teaching genetics, despite a growing need for these services. Residency program requirements for genetics competency are currently sparse and ill-defined. As residency bridges the educational process between medical school and clinicianship, we expect that residency programs need to be targeted for improving genetics education. The National Coalition for Health Professional Education in Genetics (NCHPEG) provides a set of guidelines for core competencies in medical genetics that all physicians should possess, and medical residency may be the best time to address these topics.

OBJECTIVES

The purpose of this project was to determine the current status of genetics education in residency programs by submitting a survey to program directors. This survey would help to identify genetics topics that are considered essential information for residents in various medical specialties, with the intent to generate an educational program to address these topics.

METHODS

An 81-item Google survey was submitted to directors of all residency programs accredited by the Accreditation Council for Graduate Medical Education (ACGME). Our analysis will focus on four major specialties: medicine, obstetrics/gynecology, pediatrics, and surgery. In the first section, the survey lists a general selection of genetics topics and disorders and asks directors to indicate whether the topic is relevant to and/or addressed by the program curriculum. The second section asks directors to describe the extent of genetics education in their curriculum and which teaching methods are currently used or potentially effective in the future. The final section allows directors to provide additional comments on genetics topics relevant to their specialty that should be addressed. Our analysis will be performed on a total of 35 survey responses and results are pending.

CONCLUSIONS

Survey data will be used to assess the current status of genetics education in the specialties of interest and determine which topics are considered essential to each field. We expect to find common trends in perceived deficits in medical genetics education amongst these residencies and will use this information to generate an educational program to address these needs.

REFERENCES

A Focus Group Evaluation of a Text Messaging Program to Raise Awareness about Self-breast Exams

Washington, DC has the highest mortality rate of breast cancer in the nation. Awareness of preventative screening measures and early detection is vital to early diagnosis and survival. The George Washington University Cancer Institute (GWCI) has implemented a text messaging program (TEXT4BSE) to increase breast health awareness of African American women in DC. It is designed to teach women about the importance of getting to know their bodies by prompting enrollees to conduct monthly self-breast examinations. The goal of this study is to improve retention, better meet the educational needs of the enrollees, and increase the rate of self-breast exams of enrollees in a preventative breast cancer text messaging service. A focus group of 14 women from the target group was held and the findings were qualitatively analyzed. Data was first organized into groups and then labeled. Participants showed great interest in using the text messaging service; however, no one within the group was currently enrolled. The groups’ comments were compiled into themes. There was high agreement that a text messaging service with educational content and breast self-exam reminder was useful and important. Most participants would join the program. Regarding message delivery, the group commented on ideal message frequency 1-2 per month. The older participants had preference of an interactive voice response system over text. The group consensus was that message content should be personalized, have an identifiable and credible sender, and messages should be specific, detailed, factual, and relevant. Incorporating a response and confirmation system for reassurance, moral support and scheduling appointments was also considered important. Some target populations for preventative health education may find text messaging programs beneficial. Focus group evaluation of message delivery, message content, and desired interactivity with the messaging system may be useful to program administrators to ensure value to the end user.
BACKGROUND
Diseases and conditions affecting the head and neck are commonly seen in the outpatient, primary care specialties. These conditions can represent up to 25-30% of daily outpatient visits in pediatrics and internal medicine. Despite this workload, exposure to clinical Otolaryngology is minimal in many medical schools. The purpose of this study was to access comfort levels in managing common head and neck disease during the four years of medical school and the three years of primary care residency. Furthermore, we aim to access where participants would refer these hypothetical patients if they were not comfortable with their management.

METHODS
This was a cross-sectional survey conducted using Survey Monkey (www.surveymonkey.com) of George Washington University Medical Students (N=256), George Washington University Medicine Residents (N=15) and Children’s National Medical Center Residents (N=50). Data was analyzed with Microsoft Excel.

RESULTS
Survey results are represented by the percentage of responses per level of training so that all years can be compared despite differences in the number of respondents. Throughout all years, the highest percentage of “Very Comfortable” responses were in the management of rhinitis/seasonal allergies (95% of PGY3 residents) and the lowest percentage of “Very Comfortable” responses were in the management of Tracheotomy care, Persistent Salivary Gland Swelling and Sudden Hearing Loss (<10% of each year). Among all years, the majority of respondents would refer all conditions to an Otolaryngologist with the exception of Cleft lip/palate (Plastics), Sleep Apnea (Pulmonology), Stridor (Pulmonology), Vertigo (Neurology), Facial Nerve Paralysis (Neurology), Rhinitis (Other) and Thyroid Nodules (General Surgery).

CONCLUSIONS
Although there is a correlation between year of training and comfort in care (farther along in training correlates to higher level of comfort), there remain a number of conditions that even the highest level of training (PGY3) do not feel comfortable treating (Tracheotomy care, persistent salivary gland swelling and sudden hearing loss, among others). Also, some conditions that the majority felt comfortable treating earlier in their training, suddenly become less comfortable (foreign body in nostril, cleft lip/palate). In addition, although there is much debate as to which specialty is “best fit” to handle complicated management of the surveyed diseases, there tends to be a consensus across all training levels.
EDUCATION/HEALTH SERVICES

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Impact of Training Modality on Advanced Cardiovascular Life Support Performance

OBJECTIVES/BACKGROUND

Survival from cardiac arrest is improved when care is provided by Advanced Cardiovascular Life Support (ACLS) trained providers and the ACLS course has become the worldwide standard for resuscitation training. Skills performance, in real resuscitation scenarios, has been poor in both the in- and out-of hospital settings, while the demand for e-learning modalities has been increasing. Our study was designed to evaluate the learning outcomes of two variations of ACLS training, in first time ACLS students, within the context of cognitive knowledge acquisition and skills performance.

METHODS

Previously untrained nurses and physicians (n=223) were trained in Advanced Cardiovascular Life Support using either the traditional, two-day course format or the computer based HeartCode ACLS (Laerdal Medical) training tool. Each provider was randomized to either the traditional course or HeartCode program and examined prior to receiving training materials, after completing training, and at 3 and 6 month intervals after their training.

RESULTS/CONCLUSIONS

While both training modalities resulted in significant improvements in post course written examination scores, the traditional course was superior to the PC based course in both written exam scores (93% vs. 89%, p<0.02) and megacode exam scores (84% vs. 46%, p<0.01). Our study demonstrates the critical role of hands on training in developing the psychomotor skills necessary to provide competent ACLS care in providers taking the course for the first time.
ASSOCIATES

Assessing Total Pain in the Emergency Department

BACKGROUND
The term “total pain” refers to both physical and non-physical pain and has been described as the multiple, interconnected dimensions of pain and suffering that occur for those who are experiencing end-of-life. However, total pain is not confined to end-of-life experience. Current studies of total pain are exclusive to palliative, chronic or primary care settings. No studies exist that examine how total pain is assessed in the Emergency Department (ED).

STUDY OBJECTIVES
1) Observe how patients present pain and how clinicians assess pain in the emergency department in order to 2) examine the current pain assessment tools and techniques and 3) discover if non-physical pain is measured or accounted for in the pain assessment process.

METHODS
As a pilot study, data was collected over an eight week period which resulted in 30 observations of the clinical encounter between patients and clinicians. Semi-structured interviews were conducted about the numerical rating scale (NRS) and perceptions of physical and non-physical pain.

RESULTS
The widely used Numerical Rating Scale (NRS) of 0 to 10 was found by clinicians to be insufficient for assessing physical pain and does not address non-physical pain. Eleven out of 12 clinicians had ideas for how to improve pain assessment in the ED, some of which included informal techniques for how to assess non-physical pain. The common goal among patients and clinicians in the ED was to eradicate pain; but it was discovered that patients and clinicians had different and often competing motivations for pain relief sometimes leading to unproductive clinical encounters. Patient motivations were 1) eliminate pain, 2) eliminate fear of the unknown, 3) be believed or validated by the clinician, 4) be seen faster and 5) seek drugs. Clinician motivations were typically 1) to rule out patient exaggeration or untruth, 2) follow The Joint Commission (TJC) regulations, 3) see patients quickly and 4) avoid overmedication. The key to bridging the gap between competing motivations in 100% of the productive encounters observed was when patients felt their pain was validated/believed by the physician or physician assistant (PA). The data suggest that physicians and PAs may best be equipped to validate patients’ total pain because patients perceive them as the treatment decision makers.

CONCLUSIONS
The pain assessment model in the ED needs to address total pain in order to guarantee better assessment of patient pain and to bridge the gap between the competing motivations of clinicians and patients; which could eliminate unproductive ED clinical encounters.
Humanism in Medicine: A Qualitative Study of How Graduate Medical Trainees Learn Humanism

**BACKGROUND**
Practicing medicine in a humanistic fashion is fundamental to the altruistic philosophy of the profession. The Arnold P. Gold Foundation defines humanism as incorporating respect, empathy, and integrity in patient-doctor interactions. This definition is similar to the ACGME competency of “Professionalism.” Various sources have differing definitions of humanism. The aim of this phenomenological study is to understand how physicians in training define, experience and practice humanism in medicine. These investigations can then inform medical education strategies.

**METHODS**
Recruitment: Although undisclosed to recruits, invitations to participate were extended based on recommendations from residency program directors.

Participants: A total of 14 residents (7 OB/GYN and 7 Internal Medicine) agreed to participate in 60 minute interviews.

Data Collection: Two residents conducted the one-on-one interviews with participants. The interviewers had no professional supervisory relationship with any resident they interviewed. Interviews were conducted in a private setting removed from the resident’s usual workspace, and were tape-recorded for later transcription.

Data Analysis: Data were analyzed using the Moustakkas method for coding and thematizing. Investigator triangulation, peer debriefing, and peer code checking were used to ensure consistency of findings.

**RESULTS: TEXTURAL**
Humanism involves altruism, ethics, empathy, and accountability. The process of learning humanism involves vulnerability and self-disclosure, and is supported by mentors who “encourage in public and confront in private.” Patient noncompliance is a common source of frustration, although most participants ascribe noncompliance to physician failure to communicate or to a tension between priorities.

**RESULTS: STRUCTURAL**
Following the golden rule is the essence of the definition of humanism. Humanism is learned in more than one manner, including upbringing, personal or family experience with illness, role-modeling, and story telling. Humanistic behavior sometimes “comes naturally,” yet specific behaviors may be modeled and learned. The learning process requires intrinsic motivation. Personal, social, and societal expectations motivate residents, and these expectations are sometimes experienced as pressures. The dynamics between attending, resident, medical student and patient all play a role in forming a “circle of trust” required for practicing humanism.

**CONCLUSION: COMPOSITE**
Humanism is more than knowledge and competence. Humanism involves engaged communication and intimate sharing. It is mimicked at first from early family experiences and then emulated via role-modeling before being internalized. Humility is fundamental to humanism. Respect and trust amongst teams and colleagues helps cultivate the introspection and vulnerability required for skill development. Residents consider humanism to be distinct from professionalism.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

The “Teaching Resident:” A Model for Leadership Development and ObGyn Residents Experience

OBJECTIVE

Residents are estimated to provide up to 70% of the clinical education received by medical students. In the ObGyn Department at George Washington University Medical Center, a specialized program is in place for teaching 3rd year medical students. There is a designated “Teaching Resident” (TR) assigned to organize weekly teaching conferences for the medical students, be the students’ main contact person, arrange the students’ schedules and provide any additional support as required. This is a concept that is not widely practiced in ObGyn clerkships. The purpose of this study is to evaluate the experience of the ObGyn residents as the “Teaching Resident” in terms of the perception of the experience, what the residents learned from the experience and how the residents have incorporated the experience into practice.

STUDY DESIGN

The study is composed of a survey of 13 questions.

RESULTS

20 senior residents were surveyed. Residents rated the TR experience as a source to teach professionalism skills as 4/5; as a means of educational value 4/5. Average time spent in preparing for lecture was 28 minutes. 76% of residents would implement the TR program if they were responsible for medical student education. As a whole, the residents rated 2.4/5 for the amount they learned from student presentations, but gave 3.8/5 for the educational value derived from their own presentations. The most common benefit listed included “teaching experience” and becoming a “role model”; most common complaints were “time spent” and “creating schedules.”

CONCLUSION

Residents are a major resource in teaching medical students in our specialty. In the TR model, the medical student benefits from learning in a supervised, structured environment. Additionally, the resident learns how to become a skilled and effective leader as substantiated by our survey.
The George Washington School of Medicine & Health Sciences Gross Anatomy: A film introducing first-year medical students to the Gross Anatomy experience

BACKGROUND
In the past, students entered the gross lab with little preparation and without an opportunity to process what for many is a profound and sometimes disturbing experience. They were shown a video with experiences and reflections of faculty, students, and donors from a Texas medical school on death, dying, and dissections.

PURPOSE
The project’s aim was to improve the first-year medical student’s experience in the Gross Anatomy lab and to challenge students to begin to think about death, dying, and professional detachment in the context of medicine. We chose to create a video to present the information. The objectives of the film were for students who have watched it to be able to (1) understand how the Body Donor Program works, (2) describe how the Gross Anatomy Lab functions, (3) identify what is expected of them in lab, and (4) appreciate the reflective component of the lab experience.

METHODS
The images, reflections, stories, and ideas in the video introduced first-year students to our gross anatomy lab, our faculty, our students, and our donors. The video content selected for the film was based on faculty and student feedback from previous Reflection on Gross Anatomy sessions, resources from other medical schools, and published literature supporting effective medical education techniques. A questionnaire was created to gauge how well the video met its objectives.

RESULTS
The completed video was shown to first-year students in a classroom before entering the gross anatomy lab for the first time. Seven weeks after beginning gross anatomy, first year students were given the questionnaire to assess how helpful the video had been in preparing them for gross anatomy lab (assessment of results is in process).

LIMITATIONS
We recognize that a pre/post retrospective questionnaire does not provide an adequate control group to quantitate any effect due to watching the video. Pre/post retrospective requires students to think back to before they saw the film, which introduces bias that could be eliminated with a control arm. Ideally, students should take the questionnaire before watching the film and then after to determine group differences. Also, timing of the questionnaire may need to be fine-tuned so that students have had enough exposure to the lab to accurately rate the video’s impact on their experience.

CONCLUSIONS
We believe that this formal introductory approach to medical education in the gross anatomy course has the potential to enhance the anatomy experience of students at GW.
The purpose of this project was to incorporate the use of integrative medicine modalities among first and second year medical students to promote overall well being and further their understanding of the field of integrative medicine.

An 8-week therapeutic yoga program was offered for all students of medicine and health sciences in the fall of 2010. A therapeutic yoga teacher taught the course with emphasis on self-care, mindfulness, and applications for patients in healthcare settings. The 8 week course cost 80 for students, and students were asked to commit to the full 8 weeks. Students were given an option of coming to lunchtime or an evening class. Classes were held in the main building of the medical school. In the fall of 2011 this course became an official elective of the School of Medicine, with 35 students completing the 8 weeks. In the spring of 2011 a 6-week community acupuncture clinic was offered for second year medical students as they prepared for their Step 1 board examinations. Students were given one-hour acupuncture treatments by two acupuncturists at the GW Center for Integrative Medicine in a communal setting across the street from the medical school. Students were asked to commit to the 6-week course and paid 20 per session or 120 for the 6 weeks. There were 25 students who signed up for the therapeutic yoga class, with about 15 coming each week. Students registered from across the disciplines of medicine, public health and physician assistant programs. The community acupuncture program was offered to a maximum of 6 students, every spot was filled, and all six students attended the full 6-week program. The community wellness initiative provided an affordable and accessible means for medical students to access integrative medicine modalities. The exposure and experience of these programs provided a self care model that promotes further understanding of the application of integrative medicine modalities among medical students.
Using patient simulation and educational strategies to improve physical therapy student proficiency, patient safety and outcomes in pre-hospital management of patients with medical emergencies

BACKGROUND
Physical therapists play an increasingly vital role in the identification and management of medical emergencies in patients, including pre-hospital care of athlete patients and through physical therapy care in emergency departments.1-3 Simulated patient scenarios are well-established, successful teaching and learning tools in clinician education, and have also been used to identify curricular gaps.4-9 The purpose of this study is to identify areas of strength and weakness in physical therapy students (SPT) and emergency medical technician students (S-EMT) skill-set in the management of patients having a medical emergency

METHODS
Second-year Doctor of physical therapy students were placed in a standardized simulated patient scenario in which a medically-complex patient underwent an evolving medical emergency requiring management and transportation to a hospital by S-EMT. SPT and S-EMT were graded using rubrics that identified necessary steps for the appropriate management of the scenario. SPT and S-EMT students also completed questionnaires that qualitatively explored self-perceived strengths and weaknesses. Several days after the encounter, SPT and S-EMT participated in group discussion using the critical incident stress debriefing format. 10 The encounter was videotaped for the purposes of reflection and discussion.

RESULTS TO DATE
Data collection is in process for this project. However, early reflection and discussion of preliminary emergency scenarios reveal that SPT and S-EMT report low levels of confidence and knowledge in managing emergencies in patients.

Contd on next page
CONCLUSIONS

Based on student discussion and faculty observation, teaching and simulation modules for managing emergencies in patients in the physical therapy setting will be valuable in increasing the knowledge, skills, abilities and confidence of SPT and S-EMT. Results from this project will guide future research and curricular development in this emerging area of physical therapy clinical practice.

REFERENCES


Global Health pandemic response can be a wasteful expenditure both economically and in terms of long-term outcomes in Environmental Health. Specifically, this waste generated in remote areas results in a variety of potential issues. WHO has created disinfectant agents, rodenticide, pesticide, and insecticide mandates for an contagion event, yet the use and subsequent disposal of these contaminants have not been extensively studied. This report set out to find the toxicological impact of waste generated from remote and third-world areas, and specifically was focused on both the environmental and human impact of each of these chemicals. This measure was first done by chemically evaluating noted disinfecting agents, rodenticides, pesticides, and insecticides in a qualitative risk assessment. The dose response and exposure data for these compounds were then regarded in order to place these in qualitative hazard potential. The overall assessment was then placed under a qualitative risk assessment, and thereby qualitatively presented in terms of the proper risk management tactics for each of the individual chemicals present.
BACKGROUND
In response to the growing concern about urban pest and pesticide exposures, the Washington D.C. Department of the Environment funded a team to assess the District's pesticide regulation and education needs. The effort resulted in the 2008 Washington D.C. Pest and Pesticide survey. The survey was conducted because almost nothing was known about pest problems and pesticide use among urban residents.

OBJECTIVE
The primary objective was to develop recommendations that could strengthen efforts to protect the public from pests and pesticide exposures. We focused on identifying trends in pesticide use among households with children because pesticide exposure may lead to severe health consequences.

METHODS
Surveys were completed with approximately 100 participants from each of the eight D.C. Wards. We collected and analyzed data and reviewed pest control practices in order to develop an effective children's health and pesticide program.

RESULTS
Many respondents with children in their household reported engaging in practices that pose a risk to children's health. This was true for all Wards and income levels. For example, 65% did not keep pest sprays in locked storage and 40% did not read the label. Furthermore, respondents in all Wards only reported a moderate knowledge of pesticide safety, but almost 90% reported wanting to learn more about safe practices.

CONCLUSIONS
Education, outreach and integrated pest management are critical to prevent harmful pesticide exposures, particularly where children are present. However, the legal system can also be used to encourage pesticide manufacturers to develop safer products and improve regulation of pesticides.
ENIRONMENTAL SCIENCE

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Integrating Occupational Health Impacts into Life Cycle Assessment

BACKGROUND
Life cycle assessment (LCA) is a systems-based method for evaluating environmental impacts across a product’s life cycle (i.e., raw material acquisition, manufacture, use, and disposal). LCA applications include decision making, identification of process improvement possibilities, and communication (e.g., eco-labeling). Because LCA evaluates environmental impacts alone, its applications may result in problem-shifting where a solution resolves an environmental challenge but results in unintentional impacts to occupational health. This research proposes a work environment-LCA (WE-LCA) method to assess occupational health impacts and evaluates the method using a case study in municipal solid waste (MSW) management.

METHODS
An indicator of work environment impacts was developed based on the disability-adjusted life year (DALY). The work environment-DALY (WE-DALY) was estimated using publicly-available information from the U.S. Bureau of Labor Statistics. The indicator was then incorporated into a life cycle assessment model designed to characterize both human health and occupational health impacts. The model was built to conform with the processes common to MSW management (e.g., collection, sorting, and management via incineration or landfill methods).

RESULTS TO DATE
The worker health impacts from the WE-LCA are significant in comparison to the human health impacts from LCA. This suggests that the LCA, which lacks worker health impacts, only views part of the overall impact to human health. In addition, the industrial processes contributing to worker health impacts (e.g., injuries sustained during transport of MSW) were different from those contributing to human health impacts (e.g., landfill methane emissions impacting climate change). Conclusions: The LCA method is a more holistic view of overall health impacts with the addition of the work environment. Impacts to occupational health and safety are comparable to human health impacts and should be included in all future life cycle evaluations. The WE-DALY is proven to capture occupational health and safety impacts across a product’s life cycle. Also, the WE-LCA method provides users with information about the processes contributing to the impacts and the industries with the largest impacts. This information is important and useful in decision-making and trade-off analyses.
Association between perceived union connection and upper body musculoskeletal pains among unionized construction apprentices

BACKGROUND
Several studies show varying associations between unionization and workers’ health and wellbeing. This study investigated the association between individual worker’s perceived union connection and musculoskeletal pains (MSPs).

METHODS
We conducted a cross-sectional survey of 1,757 unionized construction apprentices. Perceived union connection is a psychosocial scale measured by six questions that assessed individual worker’s connection to their union (range 10 to 24) at unionized workplaces. We measured the prevalence of four MSPs (neck, shoulder, arm, and back pain) and difficulty in daily home activities, job activities, and sleeping caused by each of the four MSPs.

RESULTS
We found that a one score increase in perceived union connection was associated with 5% decreased odds of reporting neck pain (OR: 0.95, 95% CI: 0.91 – 1.00) and back pain (OR: 0.95, 95% CI: 0.91 - 0.99) after adjusting for confounders including self-reported ergonomic strain. We also found significant associations between perceived union connection and MSPs causing difficulty in daily activities. For a one score increase in perceived union connection, the odds of reporting back pain causing difficulty in home activities, job activities, and sleeping was 9% (95% CI: 0.87 - 0.96), 8% (95% CI: 0.88 - 0.96), and 7% (95% CI: 0.89 - 0.98) lower, respectively.

CONCLUSIONS
Although our findings are limited by the cross-sectional nature of the data, these results suggest that workers’ perceived union connection can vary even within unionized workplaces, and it may be associated with the prevalence of MSPs and MSPs causing difficulty in daily activities.
The effects of confined poultry feeding operations on discharges of antimicrobial-resistant pathogenic E. coli and nutrients from watersheds

BACKGROUND

There is growing public health concern over the contribution of agricultural antimicrobial use to the rise in drug resistant bacterial infections in humans. In U.S. poultry production, antimicrobials are permitted as additives to feed or water and it is estimated that nearly 80% of poultry farms in the U.S. use antimicrobials in feed. The U.S. raises approximately 8.7 billion broiler chickens annually, resulting in an estimated 13–26 million metric tons of poultry litter. Poultry litter has been found to contain large amounts of antimicrobial resistant bacteria and resistance genes associated with the use of antimicrobials in poultry production. This has raised concern for environmental dispersal of antimicrobial resistance as nearly 90% of poultry litter is applied to land untreated.

OBJECTIVE

The specific aim of this study is to compare extraintestinal pathogenic E. coli – a major source of morbidity and mortality in the U.S. – in several streams draining watersheds with contrasting levels of intensive broiler chicken production in the Chesapeake Bay basin.

METHODS

We will compare stream water quality discharged from eight agricultural watersheds, four in the area with high densities of poultry and four in area with low densities. Water samples will be collected during all four seasons during base flow and following rainfall events in the selected streams from late February to October during 2012. Microbiological analyses will be conducted to determine whether extraintestinal pathogenic E. coli are present in watersheds populated by large numbers of poultry operations. We will also characterize drug resistance profiles of the E. coli isolates.

RESULTS TO DATE

The research team has selected watersheds for inclusion into the study and will begin collecting microbiological samples in February 2012. Future Directions: Future research will aim to apply novel analytical methods – mainly molecular microbiological analyses – to improve our understanding of how poultry operations are affecting the Chesapeake Bay in terms of microbiological contamination.
There has been a steady increase in the number of reports of aircrafts exposed to lasers directed from the ground. In the first six months of 2011, there were 671 cases reported to the Civil Aviation Authority of the United Kingdom (UK CAA) and there have been many thousands more worldwide. While the likelihood of any injuries directly resulting from laser exposure is currently extremely low, the increasing power of available lasers raises the possibility. A project was undertaken to develop a rapid self-assessment tool to assist in determining if permanent injury has occurred after eye illumination from a laser and whether professional treatment should be sought. The Aviation Laser Exposure Self-Assessment (ALESA) was then evaluated using a population of pilots who had experienced illumination.

Methods
The project included a literature review, a study of laser incidents reported to the UK CAA, and a discussion with experts and individuals who had experienced illumination. The ALESA was produced using the key aspects of illumination that are important to determine the risk of harm. An Amsler grid was included to enable quick self-assessment of vision. A study was undertaken using a questionnaire with a five point Likert-type scale to assess the attitudes of pilots on the use of the ALESA. The study population consisted of 25 male and female pilots and flight crew members who have experienced aviation laser beam exposure.

Results
Content validity was established by the expert’s judgment of the appropriateness of the ALESA and face validity was found by the participant’s responses. The proportion agreeing (responding favorably) was found to be significant for most aspects of the ALESA.

Discussion
The ALESA was shown to be of use to the aviation community and the UK CAA is currently making the tool available within the United Kingdom. None of the participants experienced any laser-related damage from their exposure, and the probability of such damage at this time is extremely low. As the power of lasers purchased by the public increases in the future, it will be desirable to establish the sensitivity and specificity of the ALESA.
Management of Multidrug and Extensively Drug-Resistant Tuberculosis in Peru: A Qualitative Study in Urban (La Victoria, Lima) and Rural (Ucayali) Sites

Problem
Peru accounts for 3% of the Latin America and the Caribbean (LAC) region’s population, but 12% of the region’s tuberculosis (TB) and 17% of the region’s multidrug- and extensively drug-resistant tuberculosis (M/XDR-TB) cases. Peru’s acclaimed National TB Program (NTP) has high levels of DOTS (directly observed treatment short course) coverage; however, the country’s decline in incidence rates has recently slowed down. While TB treatment is among the most cost-effective health interventions, recent studies show that DOTS leads to a rapid decline in incidence only over a short period of time. Studies also show that although some DOTS’ components are useful, its assessment in combination with additional programmatic components may be needed to attain sustained declines. Assessing Peru’s NTP could identify DOTS suitability and missing additional components for a sustained decline in the incidence of TB and M/XDR-TB.
Time trends in diarrhea mortality in Mexican children under-5: the population effect of various interventions including water, sanitation, and the rotavirus vaccine

BACKGROUND
Diarrhea is the second leading cause of childhood mortality in children under-5 worldwide causing up to 1.3 million deaths annually, many of which can be prevented by simple measures including oral rehydration therapy (ORT), access to improved water and sanitation, and the rotavirus vaccine. In Mexico, diarrhea deaths in children under-5 have decreased dramatically over the past 3 decades. We quantified the mortality reduction associated with the introduction of various public health interventions over time.

METHODS
Monthly mortality data from 1979-2009 from Mexican children younger than 5 years, obtained from Mexico vital statistics, was examined. A diarrhea death was defined as any mention of an ICD code for diarrhea (corresponding to ICD10 codes: A0-A09). Mortality rates were calculated for summer and winter seasons, using population census data for denomination.

RESULTS
The mortality rate decreased by 96% in infants and 94% in toddlers (1-4 years) over 3 decades. A distinct seasonal pattern with dramatic summer peaks in the early years was observed, consistent with bacterial diarrhea, but by early 1990s the summer peaks had nearly disappeared, revealing modest winter peaks, temporally consistent with rotavirus seasonality in Mexico. The effect of public health interventions of diarrhea mortality revealed that ORT introduction in 1984 was associated with an average annual decrease of 58.8/100,000, improvement in water and sanitation in 1989-1999 was associated with an average annual decrease of 30.5/100,000, while introduction of the rotavirus vaccine in 2007 was associated with an annual decrease of 6/100,000. ORT and improvements in water and sanitation dramatically reduced summer mortality whereas the rotavirus vaccine primarily affected winter mortality.

DISCUSSION
The Mexican success, eliminating most diarrheal deaths in young children, can help inform policy makers in other middle and lower income countries. The introduction of ORT, water sanitation and other improvements relating to Mexico transitioning from lower to a higher middle income GDP reduced under-5 diarrhea mortality by 40-fold. In contrast, the introduction of the Rotavirus vaccine, while halving the residual winter diarrhea mortality, contributed only modest to the overall reduction in diarrhea. Had the rotavirus vaccine been introduced around 1980, the maximum reduction would have been around 18%, as only winter deaths can be prevented. When considering introducing the rotavirus vaccine in countries in various developmental phases, it is critical to weigh the costs of such a program against the cost of introducing more universal diarrhea reduction strategies that would address both summer and winter diarrhea.
Mobile health, also referred to as mHealth, is an expanding field that utilizes mobile technologies to improve health outcomes. A great opportunity exists in low-middle income countries to employ mHealth because of high rates of penetration of mobiles, even for those at the bottom of the pyramid. There is an ongoing debate regarding the effectiveness of mHealth interventions, particularly because there is a dearth of robust evaluations of mHealth interventions. The World Health Organization has identified six building blocks of overall health systems. These include: Leadership and Governance, Health Workforce, Health Service Delivery, Health Financing, Health Information Systems and Medical Equipment and Supplies. By strengthening each individual block and the interactions between the blocks, overall health systems may be impacted to improve health outcomes. The intersection of mHealth interventions and the health system can give greater insight into whether or not mobile technologies are being utilized in a manner that impacts overall health outcomes. This is a systematic literature review of 11 peer-reviewed articles outlining evaluations of mHealth interventions that intersect with one or more of the WHO’s accepted building blocks of health systems were examined. The quality of each study was based upon five characteristics, which include the feasibility of the intervention and robustness of the evaluation design. There were notable patterns between the type of mHealth intervention and the health system building block that was impacted, and clear barriers were identified that lessened the impact and scale of the interventions. Recommendations to improve the effectiveness of mHealth interventions through the strengthening of overall health systems include: rigorous and relevant evaluation designs; implementation of business models; building uniform methodology that links mHealth interventions to health systems building blocks; creation of guidelines and best practices; and, ensuring that all relevant actors, organizations and partnerships are involved in the design and implementation processes.
The Epidemiology of Dengue Fever in St. Lucia: Examining the Increase in Incidence from 2006 through 2011

BACKGROUND

Dengue fever, a vector-borne disease endemic in most countries located throughout the tropics, affects 2.5 billion people in over 100 countries. During the past three decades, the Latin America and Caribbean region has confronted cyclical outbreaks of dengue fever occurring every three to five years, with the last major outbreak occurring between 2007 and 2008. Between late-2010 and 2011, the Caribbean island of St. Lucia experienced a dramatic increase in the number of reported cases of dengue fever, potentially associated with increased rainfall from extreme weather, which may influence the breeding habits of the Aedes aegypti mosquito. This study seeks to determine how extreme weather contributes to the increasing incidence of dengue fever in St. Lucia.

METHODS

Weekly reports sent to the St. Lucia Ministry of Health from all regional health centers and hospitals were collected and analyzed using Microsoft Excel 2007 to determine weekly total cases, averages, etc. Finally, RAR database files of annual rainfall data provided by the Meteorological Offices of St. Lucia were analyzed using Microsoft Excel 2007, and compared to the incidence data. Results: St. Lucia reported 758 confirmed cases of dengue fever in 2011, which is a significant increase from 2010 with only 96 confirmed cases. In 2010 and 2011, three serotypes of dengue fever were identified, along with 23 confirmed cases of dengue hemorrhagic fever. Also in 2011, there was an unusual increase in the number of cases of undifferentiated fever (7809 cases reported versus 2875 cases in 2010), which may indicate an increase in reporting of cases.

CONCLUSIONS

This analysis indicates that the incidence of dengue fever cases is on the rise, and cases are occurring outside of the normal time of year when they are expected. The unusual increase in the number of reported cases in the month of November 2010 (20 cases) may have been the result of the impact of Hurricane Tomas on mosquito breeding sites; hence the reemergence of cases in November 2010 that is observed after the decrease in cases in October 2010. This study on dengue fever in St. Lucia is relevant and timely, and presents important issues facing many developing nations today: controlling emerging infectious diseases, advancing epidemiological research, and establishing long-term national policies for addressing these health issues.
GLOBAL HEALTH

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

The burden of tuberculosis among migrating populations and slum settings: A systematic review and meta-analysis

OBJECTIVE

To assess the burden of tuberculosis among migrating populations and in slum settings, as well as describe the challenges, approaches and recommendations for TB control in these settings.

METHODS

A systematic review and meta-analysis of published reports was performed. Using strict inclusion criteria, four databases were searched for published literature, complemented with a grey literature search. All included articles were assessed with a quality checklist. Quantitative and qualitative analysis methods were employed. Odds ratios were calculated for studies reporting TB cases in slum settings, using national TB incidence as a comparison. A combined summary estimate was calculated, using the random effects model (95% confidence intervals for each study). Studies reporting the burden of TB were analyzed based on the TB case definition, method of case finding, and risk factors that could increase TB rates. The challenges, approaches and recommendations for TB control were assessed qualitatively.

RESULTS

A total of 25 studies were included in the review: 12 reported the burden of TB, 3 discussed the challenges, 4 on approaches to TB control, and 6 studies presented recommendations for TB control in migrating and slum settings. Compared to national TB incidence rates, the combined odds of pulmonary TB within a slum setting was not statistically significant across studies, however the combined odds of smear positive TB, smear positive TB with active case finding, and smear positive TB in a high HIV slum setting were statistically significant in slum settings. Challenges of TB control within slum settings include treatment non-adherence, lack of knowledge about TB, and safety concerns of health workers. Approaches to TB control include the TB Manyatta project, a defaulter-tracing program, and a community advisory board for TB. Recommendations suggest changes in policy, education, and overall health system integration and multi-sector involvement.

CONCLUSIONS

The odds of TB are at least 3 times as high in slum settings and recognition of this issue is the first step in reducing the global burden of TB. Recommendations include: global recognition of slum settings as formal establishments; regional collaboration for TB control; and increasing visibility of the TB burden among migrating populations through the Global Plan to Stop TB.
Global Health

School of Public Health and Health Services

Environmental and behavioral risk factors for cholera transmission during a 1993 outbreak in the Gilgit-Baltistan region of Pakistan

Objective

We conducted an analysis of epidemiological data collected in the context of a 1993 cholera outbreak in the Gilgit-Baltistan region of Northern Pakistan. We investigated the spread and risk factors associated with the epidemic, identified behaviors impacting vulnerability, and sought to evaluate the effectiveness of ORS and vaccination. The results are intended to help appropriately focus intervention efforts for future outbreaks in the region and globally.

Methods

The analysis was conducted using three original datasets collected by researchers during the outbreak. One was a case-control database of 105 cases and 142 controls collected in eight villages. Also, a cross-sectional survey interviewing heads of households about all recent diarrhea cases was assessed. The third consists of a case-control dataset based on all hospitalizations for diarrhea that occurred during the outbreak period. Cholera cases were defined as >10 watery stools per day, clinical or laboratory diagnosis of cholera, as well as absence of bloody diarrhea or differential diagnosis. Data was entered and analyzed using SAS. Univariate analysis and multiple logistic regression were used. Analyses were conducted on each dataset separately since patients could not be linked.

Results

Most households used pit latrines, few disinfected their drinking water and most had not finished elementary schooling. Within case-control analysis, low education (OR 2.3, p<0.04) and eating fresh fruits or vegetables (OR 2.69, p<0.04) were associated with cholera. Furthermore, use of the channel as a water source (OR 0.25, p<0.002) and washing hands after defecation (OR 0.34, p<0.02) were protective factors, whereas treating water was not significant. Approximately 16% of individuals in the household survey and 44% of individuals in the hospital dataset met the cholera case definition. Vomiting, absence of fever and being over 5 years of age were associated with cholera.

Conclusion

This study examines an epidemic that appeared in an area previously unaffected by V. cholerae. In contrast to the largely pediatric nature of cholera in endemic areas, this outbreak affected adults more than children. Our findings emphasize the protective effect of education, and the need for improved water sanitation and hygiene practices to control cholera. While vaccination was implemented in the context of the outbreak response, too few patients were vaccinated before their illness onset for us to evaluate the benefits. The swift intervention by local health authorities, including proper surveillance, likely helped limit the outbreak.
Using Multiple Case Studies to Understand Drivers of Routine Immunization Performance in Sub-Saharan Africa: a review of the synthesis analysis process

BACKGROUND & OBJECTIVE
This study presents the synthesis of three case studies conducted by the Africa Routine Immunization System Essentials (ARISE) project, managed by JSI Research & Training, Inc., which aims to create evidence to inform future decisions surrounding routine immunization (RI). Cameroon, Ghana and Ethiopia were selected as case study countries for exploring drivers of RI performance in Sub-Saharan Africa, based on improved rates of DPT3 coverage between 2007-2010. In each country, data was collected from four districts: three with increases in RI coverage and one with steady coverage as comparison. The challenge for the ARISE synthesis was to create a continuum with the single-case analysis done by the country teams.

METHODS
Synthesis analysis identified patterns and themes across the 9 improving districts to formulate “common drivers of RI performance”. The case study database included: in-depth interviews, focus group discussions, observation, a National Situation Assessment (NSA), and document review. The synthesis team undertook 6 activities to ensure analytical continuity and transparency of the formulation of the common drivers. 1) A “synthesis workshop” gathered country teams to identify common themes across cases. 2) Interview and focus group transcripts were coded using NVivo software by a team from GWU SPHHS and output generated based on the common themes. 3) Country case reports were checked for analytical continuity with the synthesis formulation of the common drivers. 4) The synthesis analysis methodology was carefully documented. 5) A standard template documented the synthesis analysis process for the common drivers. 6) Country team members and RI experts reviewed progress on the synthesis.

RESULTS TO DATE
Six themes were identified during synthesis workshop; the synthesis analysis determined that four were direct “drivers” of RI performance, and the other two functioned as enablers. Synthesis findings did not contradict country-level findings, but in identifying commonalities, deviated from specifics in individual country cases.

CONCLUSION
Data was collected and analyzed for the single country cases by researchers other than the synthesis analysis team. This is a common challenge in multiple case study approaches, and can introduce methodological problems during the synthesis analysis. The synthesis process reaffirmed the value of input from country teams and RI experts to reinforce the robustness of the synthesis conclusions. The ARISE synthesis analysis provides guidance and lessons learned for other multiple case studies, which are used more frequently to understand the performance of public health programs, particularly in terms of “systems” performance.
Predictors of Intention to Become Circumcised Among Swazi Males Aged 13-29 Years

BACKGROUND/OBJECTIVES
Mounting evidence indicates the potential of male circumcision (MC) to substantially reduce HIV infection rates all over the world. Less research, however, has been conducted to identify the factors that influence a man’s intention to get circumcised. Swaziland currently experiences the highest adult HIV rate in the world and a low percentage of men who are circumcised. As a result, an opportunity exists to decrease the HIV rate in Swaziland by increasing the uptake of MC. The purpose of this study is to quantitatively assess the contextual, institutional, individual, and community factors that contribute to a Swazi man’s intention to become circumcised.

METHODS
The current study represents a secondary data analysis of a subsample of uncircumcised Swazi males from a larger study. The original sample included males aged 13-29 years residing in Swaziland. Only respondents who answered “no” to being circumcised (N=1257) were included in the current study. Bivariate logistic regression analysis was used to assess preliminary associations between MC intention and various independent variables. Multivariate logistic regression was used to determine significant predictors of intention to circumcise among the target population. Data was analyzed using STATA 11.0.

RESULTS
General beliefs, knowledge, sexual/general outcome expectations, support of friends/family for MC, and availability/access to MC facilities all predicted intention to become circumcised. Multivariate results showed that men who stated that a circumcised penis was easier to keep clean than an uncircumcised penis had 3.1 greater odds of intending to circumcise (p = .02). Those who disagreed that sex was more painful for a circumcised man had 3.2 greater odds of intending to circumcise (p ≤ .001). Men whose parents encouraged them to go for MC had 3.2 greater odds of intending to circumcise (p = .00), and men who agreed that there was a private MC clinic near them had 2 times greater odds of intending to circumcise (p ≤ .001).

CONCLUSIONS
This study emphasizes the importance that behavioral constructs have on a man’s intention to become circumcised. Knowledge and access to services are necessary but not sufficient to increasing a man’s intention for circumcision. Factors such as social support and individual beliefs should also be addressed by public health programs, which hope to increase intention, and ultimately uptake, of male circumcision.
Measuring Health Outcomes and Health Diplomacy: Some Considerations from the Field

In the last decade, the US Navy has deployed hospital ships to participate in short-term humanitarian affairs and disaster response (HA/DR) work in regions around the world. Missions entail a variety of engagement activities including general medical, surgical, dental, veterinary, reconstruction, ophthalmology and preventive medicine interventions. The recent publication of Department of Defense policy DoDI 6000.16, “Military Health Support for Stability Operations,” requires military services to develop measures of effectiveness (MOEs) that evaluate progress in achieving the goals Medical Stability Operations (MSO), including hospital ship missions such as Continuing Promise 2011 (CP11). However, there is concern among a variety of stakeholders that MOEs remain underdeveloped and in most cases unused in practice. To begin identifying gaps and best practices related to MOEs, the Office of Naval Research sponsored and funded exploratory research during CP11. The initial study question was two-fold: What is the current status of monitoring and evaluation (M&E) for MSO activities aboard USNS COMFORT that could inform the development of MOEs? And, how could M&E be improved to enhance long-term health and strategic goals? A research team, including a graduate student from GWU, embarked on the USNS COMFORT for the duration of the CP11 mission in nine countries in Central and South America. Through participant observation and semi-structured interviews, the research team interacted in local communities alongside the mission elements. In addition to researching the development of evaluative tools, the team identified new ideas for future interventions from the local community and in line with military objectives. The research process also facilitated and maintained vital relationships, which led to the expansion of the research scope beyond field-level health activities. The quantitative and qualitative impacts of this work, and the discussions that this work engender, have, in turn, affected evaluation processes of subsequent hospital ship missions. Initial results have revealed multiple gaps and opportunities for enhancing M&E efforts for both development and implementation of future evaluation tools. By working extensively both in the field and at the policy level, the team was able to demonstrate the importance of understanding the environment for key stakeholders involved in planning, implementation, and evaluation of efforts. Additionally, research and analysis identified complex and interrelated issues associated with short-term military interventions aligned to strategic military objectives. Based on these finding, the researcher(s) anticipates developing a way forward in consideration of operational realities, local environments, and the types of interventions conducted.
Development of Dengue Outbreak Forecasting Algorithm using Climate Variables as Predictors in a Syndromic Surveillance System in the Caribbean

BACKGROUND

Dengue fever is a vector-borne arbovirus. Approximately 2.5 million people are at risk of dengue infection and there are an estimated 20,000 deaths every year. Epidemiologic changes have been linked to fluctuations in temperature and precipitation, which may affect vector ecology and disease pathogens.

OBJECTIVES

By examining associations between climate variables and dengue fever incidence a surveillance system could forecast dengue fever incidence in the Caribbean. The goal of this study is to improve the predictive power of a surveillance network system for dengue in Dominica, Martinique and St. Lucia by assessing the Holt Winter’s Multiplicative Seasonality (HWMS) forecasting model, including climate variables.

METHODS

Temperature, precipitation and dengue fever incidence were collected from 2000 to 2010 in Dominica and St. Lucia and from 2005 to 2010 in Martinique. K-Mean clustering method was used to identify patterns from the datasets. Regression analysis was used to determine the coefficient between dengue fever incidence (an independent variable) and temperature and precipitation (dependent variables) in each cluster. The HWMS was modified to incorporate climate variables in the three countries. Lastly, in order to examine an appropriate public health response for using the forecasting algorithm, 1-month, 3-month, and 6-month approaches were compared.

RESULTS

Precipitation was more likely than temperature to have a positive association with dengue fever incidence during the rainy season in Dominica (0.29; p-value = 0.001), Martinique (0.038; p-value = 0.67) and St. Lucia (0.16; p-value = 0.04). The climate variables improved the HWMS model’s predictive power for dengue fever incidence in all three countries (Mean Square Error, MSE = from 1601.37 to 74.93 for Dominica, from 400.33 to 289.88 for Martinique and 964.88 to 61.83 for St. Lucia.). Moreover, the 1-month approach was recommended as appropriate for an effective and operational public health response (the average residual +5 for Dominica, +3 for Martinique, and +52 for St. Lucia).

CONCLUSIONS

Understanding an association between climate variables and dengue fever incidence could improve dengue fever forecasting. The modified Holt Winter’s model (MHW) using climate variables added value to the syndromic surveillance system for outbreak detection and early warning in the Caribbean which is currently under development. Further testing of the MHW model coupled with public health response is recommended to improve syndromic surveillance systems and help to implement robust, timely, and efficient prevention activities in the Caribbean.
Despite a flurry of literature and myriad attempts towards comprehensive definitions, measuring empowerment remains elusive. This paper uncovers correlations between survey items tapping empowerment using 2010 Malawi Women’s Status DHS (Demographic and Health Survey) data. Results are in line with empirical findings in developed and developing settings as a number of items relating to freedom of (reproductive) choice and asset endowment correlate positively with selected development and health indicators.
GLOBAL HEALTH

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

BioEconomy Africa: Gurara Women’s Development & Trade Cooperative Analysis

BACKGROUND

Disadvantaged women in Ethiopia are often characterized as having low incomes, poor health and nutrition, low access to resources, and various barriers to livelihood development. In Addis Ababa and surrounding areas, BioEconomy Africa (BEA) serves as an initiative for women to alleviate these factors by focusing on the enhancement of economic, ecologic and social capital simultaneously, through sustainable agriculture. The objective of this case study is to assess the current situation of the Gurara Women’s Development and Trade Cooperative, through community, environmental and policy lenses, and to provide recommendations to BEA about the benefits of strengthening their monitoring and evaluation systems.

METHODS

SPHHS graduate students in the Department of Global Health participating in the OLC Ethiopia program were briefed on BEA’s work, reviewed critical documents and conducted interviews with BEA staff and Gurara members.

RESULTS

A proposal was made for BEA highlighting recommendations for improved management opportunities using the Management Sciences for Health’s Challenge Model and developing a comprehensive monitoring and evaluation framework for project and grant application. This framework focuses primarily on developing nutrition indicators that were missing from past evaluation plans, and illustrating how implementation can increase the effectiveness of processes, manage improvements and help BEA qualify for additional funding. This report offers two applicable grant sources, the Global Fund for Women and African Women’s Development Fund, each which aim to empower women and advocate for human rights.

CONCLUSION

This cooperative has had beneficial effects on the livelihoods of women living in the Ferensay area of Addis Ababa, though it is not operating to optimum efficiency. Management and monitoring and evaluating design improvements need to be made in order for measurable results to be quantified and utilized to promote further improvements.
GLOBAL HEALTH

The Contribution of Global Fund HIV/AIDS Grants to the Integration of Sexual and Reproductive Health and HIV/AIDS Services in Ethiopia: results from a resource tracking case study

BACKGROUND
Integrating sexual and reproductive health (SRH) with HIV/AIDS services is hypothesized to improve both health outcomes and programmatic efficiency. In support of this international priority, the Global Fund to Fight AIDS, Tuberculosis, and Malaria (GF) encourages applicants to address SRH integration explicitly in HIV/AIDS grant proposals. The Government of Ethiopia has pursued integration since 2009, when performance on PMTCT and MNCH indicators was low. In the period 2008-2010, the two principal GF HIV/AIDS grants were re-negotiated to support this prioritization. This study examines the extent to which Ethiopia’s GF HIV/AIDS grants have contributed to SRH-HIV/AIDS activity integration.

METHODS
GF HIV/AIDS grant contribution to SRH-HIV integration was assessed by analyzing expenditures through June 2011. Expenditures for the two current grants, Round 7 and Round 2 Rolling Continuation Channel (RCC), were obtained for Principal Recipients (PRs, national-level) and Sub-Recipients (regional level). Expenditures directly and indirectly related to SRH-HIV/AIDS integration were analyzed according to the 2005 WHO framework for priority SRH-HIV/AIDS programmatic linkages.

RESULTS
Expenditure analysis indicates GF grants provide critical investment for all integration linkage areas, including: antenatal care (ANC), PMTCT, HIV counseling and testing (HCT), and condom procurement. The grants also support health systems strengthening (HSS) investments that enable integration, including information systems, human resources, and drug management systems. 100% of expenditures ($11.6 million USD) by the Round 7 primary PR were directly or indirectly integration-related, with 41% for PMTCT, and 59% in HSS categories. 89% of RCC expenditures ($26.8 million USD) were integration-related, 27% directly (50% and 24% of directly-related expenditures were for HCT and behavior change communication), and 62% indirectly (of which 91% went to infrastructure, such as health facility upgrades to enable service integration).

DISCUSSION
Ethiopia has utilized more than $38 million USD from 2 GF HIV/AIDS grants to advance integration of SRH-HIV/AIDS services in the period January 2009-June 2011. This study found that GF guidelines and grant management also have encouraged an increased focus on integration in Ethiopia, especially related to PMTCT. Several challenges involved in tracking GF resources on specific types of activities were faced, in particular variability in the availability of expenditure data by activity. This is expected given GF’s financial reporting requirements, but necessitates expenditure analysis at the service delivery area (SDA) level and approximation of how to allocate within the SDA to specific activities. This study contributes a methodology for addressing this challenge in understanding the impact of GF financial support on SRH-HIV/AIDS integration.
Ecuador’s Health Care system organizes its institutions into four major “levels”. Level placement in the health care system depends on various factors, including the institution's size and the number of medical specialties made available. Primary level institutions are located in more rural areas of Quito and act as primary care clinics. Secondary level institutions are very similar to primary level institutions, but tend to have larger capacities and medical staffs. In contrast, institutions at the tertiary and quaternary levels have the largest capacities and have more procedures available for patients (i.e., maternity hospitals, oncologic hospitals). My goal over the summer was to visit a series of medical institutions within each tier of Ecuador’s Health Care system, and to provide or assist in patient care at each of these institutions. Through this process, I aimed to gain a better understanding at each level of care.

METHODS

I worked at various medical institutions, each operating at different levels of care in Ecuador. This allowed me to have a wide range of perspectives on health care in Ecuador. The primary institution, which receives the most basic level of care, is located in Pifo, a rural parish in the metropolitan district of Quito. At the facility, I assisted physicians and other health care workers in examining infants and performing eye and dental examinations on the school children from the surrounding areas. At the secondary institutions, I assisted in the suturing of patients, cleaning of burns and wounds and performing EKGs. The tertiary and quaternary facilities, located in urban Quito, had the highest levels of care. These sites specialized in maternity care and oncology, respectively.

RESULTS

The gradient in care was marked among the different levels of institutions in Ecuador. The difference in access, sanitation, and resources was discernably lower in the rural primary institutions versus the more urban tertiary and quaternary institutions. The rural facilities focused more on primary care and traumas, such as motor vehicle accidents and falls. Tertiary and quaternary facilities were able to manage a much more complex range of cases, such as Caesarian sections and Beckwith-Wiedemann Syndrome.

CONCLUSION

The disparity in health care among different populations in Quito is associated with geographic and socioeconomic status. While a high level of care is available in Ecuador, the limiting factors to this care are largely related to financial resources and access to adequate facilities.
Schistosomiasis and hepatitis C co-infections in Egypt have led to a devastating burden of chronic and progressive liver disease in that country.

METHODS
A literature review was performed to find evidence of co-infections of schistosomiasis and hepatitis C in Egypt.

RESULTS
Schistosomiasis, a neglected tropical disease, has plagued Egypt since antiquity. During the 1900s, a mass drug administration with parenteral administration of tartar emetic was employed in an effort to eradicate schistosomiasis. It was effective; however, it inadvertently created an epidemic of hepatitis C infections. This epidemic has revealed synergies in liver disease progression resulting from the two pathogens. Several studies have shown that patients co-infected with schistosomiasis and hepatitis C suffer from an increased rate of liver fibrosis than would be present with either disease alone. Schistosomiasis triggers a Th2 cytokine response, which not only suppresses Th1 cytokine release hindering cellular and antiviral immunity, but also promotes Th2 host responses and fibrogenesis. Additional fibrogenic factors unique to the country and region include chromosome 6p23 carriers which carries a gene that encodes a connective tissue growth factor (CTGF) with stimulates strong fibrogenic molecules. Furthermore, genotype 4a predominates in Egypt and causes a higher hepatitis C RNA viral titers when compared to genotype 1 further causing a higher incidence of cirrhosis and fibrosis.

CONCLUSIONS
Egypt's co-infection epidemic is an example of how a neglected tropical disease served as an important underlying factor to the emergence chronic liver disease in Egypt. The combination of virus, parasite, and host factors appear to have created a "perfect storm" of factors leading to an epidemic of severe liver fibrosis and disease in Egypt. Accelerated fibrosis along increased disease progression has been noted in patients with co-infection of hepatitis C and schistosomiasis. There is a need for additional research to follow, detect, and ultimately halt the disease progression. More importantly, preventive measures, including health education to thwart ongoing transmission in clinics, hospitals, and elsewhere need to be fully supported to arrest the Egyptian epidemic.
GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES
Xela Healthcare

OBJECTIVES
My main goal was to observe and study general healthcare in Quetzaltenango in relation to care for the poor and care of neglected tropical diseases. Other objectives I had included improving my Spanish and also working on my medical Spanish. Ultimately my time abroad would broaden my scope of healthcare provision and make me a more empathetic and understanding physician.

METHOD
To do this I spent 8 weeks in Quetzaltenango, Guatemala this past summer living with a local family, studying Spanish every afternoon with the affiliated program Educacion Para Todos with Oscar Gomez (the owner of the school), and working every morning with a local clinic, Centro Medico Klaiss. This clinic was a private clinic for the poor and specialized in general medicine, gynecology, laboratory work, and psychology. It also had a pharmacy. I was also able to observe both the social and health culture of the city.

RESULTS
Many of the staff in the clinic was female, as were all of the physicians, so the experience was different. Many of the patients presented with problems commonly seen in urban and suburban clinics since the city is mainly urban. But what was different was the issue of payment and treatment. Because there is no insurance, everything must be paid for and can limit patient care or compliance. Also, many people have jobs that pay daily; so any therapy that involved missing work for an extended period of time was usually not followed completely, worsening outcome. There were differences in what was considered sterile or medically sound (for instance, I was taught to recap needles, we rolled cotton swabs, etc.) But I was able to give injections, nebulizers, and examine patients with the physician with my Spanish knowledge, and discuss pathology and treatment.

CONCLUSION
I found that the process of healthcare in a foreign, rural setting is usually based on economics, even though they do provide sound medical care. While I didn’t get a chance to look into NTDs, in Xela often the more common ailments, such as pneumonia or injuries, are more crippling because of the time lost from work. Also, serious medical issues, such as epilepsy, require expensive testing and treatments that many families can’t afford. So healthcare has similar but more crippling facets there than it might here in the US.
Being the first student to partake in a flagship partnership program between GWU Medical School and the University of San Pablo, CEU, requires the ability to forge your own path. The three broad goals were to conduct immunohistochemical research, gain clinical experience, and better my clinical Spanish.

Immediately, my Spanish had to improve in lab in order to communicate with the lab mates who were teaching me the techniques in Castilian Spanish. For more than a month we helped processed their samples by cutting, staining, and taking pictures on the microscope.

The Emergency Department at Sanchinarro Hospital was my first rotation. Both my colleague and I were paired with doctors in the adult arm of the ER where we practiced Spanish clinical vocabulary and delved into conversations about the Spanish healthcare system.

Towards the middle of July, I received another opportunity to do another clinical rotation in surgery. Dr. Lapuente was a general surgeon who took me on as an apprentice. He allowed me to assist when he performed surgery including a thyroidectomy, appendectomy, and a few hysterectomies. In addition, I shadowed his team when they performed several laparoscopic surgeries including a gastric bypass and more gynecological cancer surgeries. Most of these were performed at the hospital in Montepinvice, but I was also afforded and invited to shadow him perform the others at the MD Anderson Cancer Center based in Madrid.

Not only was Dr. Lapuente also worked hard to connect me to as much clinical experience as possible, most especially with whom he thought I would most learn from. A small example of these opportunities included the time I was able to watch my first birth, a c-section, and when he personally called the director of the Pediatric Oncology/Hematology group at Montepinvice to help me schedule my third and final rotation in their department.

I was partnered with Dr. Garcia and, again, was taken on as his apprentice. I learned about creating chemotherapy treatment plans and how, in fact, there was an international method of carrying them out. It was so important to not only adhere to the schedule, but to be vigilant in keeping track of blood work and urine results; whether the medication was working, affecting other systems, and how fast the chemotherapy was being excreted by the body. He exuded the importance of internal medicine and his passion for it.
GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Evaluating Socioeconomic Barriers to Care in Public and Private Healthcare Settings in Chennai, India

BACKGROUND

Very few patients in India have access to insurance, resulting in an enormous disparity in healthcare between socioeconomic classes. The purpose of this project was to assess the effect this has on access to and quality of healthcare, as well as the doctor-patient interaction.

METHOD

8 weeks were spent in both ‘public,’ subsidized healthcare settings, as well as private hospitals, in the general wards as well as the NICU, to compare the effect of cost on how patients approached their need for treatment in each setting.

RESULT

As expected, the ability to pay was the driving force in disparity in the two settings. The doctors in both settings were equally knowledgeable, but were limited by factors of cost, availability of supplies, and the patient’s own lack of medical self-awareness in the subsidized setting. The Public Health Centre had a very busy L&D ward, and often performed Caesarians and had a basic NICU, but could not administer epidurals for routine births and had to transfer very sick babies to other NICUS for care, for example. Cost was rarely ever a factor in the private setting; however, on the occasions that a very ill patient was transferred to the private setting for higher level care (this was especially so in the NICU) the overwhelming question was often how quickly they would be able to transfer back to the public health centre due to the enormous difference in out-of-pocket cost. Patients in the subsidized setting tended to present at a much more advanced course of disease, often because cost prevented them from receiving care before an abscess became severely infected or cancer symptoms became too debilitating to ignore. The effects of social hierarchy were very apparent in how patients interacted with their doctors in each setting. Patients of relatively lower social standing tended to be far more passive, advocating for themselves far less. They also tended to be limited by a lack of medical understanding of their conditions, and were far less compliant with treatment regimens.

CONCLUSIONS

The differences between these two hospitals highlight the necessity for patient education, advocacy, and the basic need for ample sterile, good quality medical supplies. In a setting that lacks insurance, cost is the biggest roadblock to quality care, and that directly impacts the outcome that patients have, by taking focus away from their medical status.
Physicians for Peace, a Virginia-based non-profit organization, aims to strengthen global health by training and empowering international healthcare professionals. Through the medical school’s Office of Student Opportunities, and with support of the Health Services Scholarship, I had the opportunity to travel to the Dominican Republic (DR) to work as a photographer and interviewer for Physicians for Peace.

My main role was to document the work of the organization, specifically focusing on the impact on the lives of the Dominican health care professionals. In the DR Physicians for Peace works in several capacities ranging from training physical therapists and technicians at a rehabilitation center, to training nurses and physicians at pediatric burn clinic. Additionally, Physicians for Peace oversees a program, Resource Mothers, that empowers local women to act as caregivers for pregnant teenagers.

My goal of the project was to unite my interests and background of global public health, medicine, Latin America, and photography. Through my experience I was able to contribute to Physicians for Peace’s publications while expanding my and readers’ knowledge about often-neglected global health issues.
GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Nyumbani Children’s Home: Summer Experience

I spent 8 weeks in Nairobi, Kenya, working with Nyumbani Children’s Home, a not for profit organization dedicated to serving the pediatric, HIV affected population of Nairobi, Kenya. Specifically, I worked through the Lea Toto outreach program, a network of health clinics that work at the grassroots level within some of the most under served areas of the city. Most of my time was spent with the clinical officer conducting patient interviews, performing physical exams, drawing blood, as well as dispensing medication.

A second focus area of my project involved the diagnostic and adherence counseling aspect of Lea Toto’s service provisions. As the gateway to these various services including healthcare, nutritional support, education, and policy advocacy, the counseling department certainly has an extensive history of experience that they continuously seek to improve upon. As part of my project, I provided an informal evaluation and proposal for the purpose of streamlining the delivery and organization of counseling services. This included incorporation of IT services and multimedia, as well as a standardization of the protocol for each clinic’s counseling program.

Care-delivery systems in developing countries are unique in general, but complemented by the backdrop of a disease like HIV certainly provides a challenging context for anyone seeking to gain or provide aid. The imperative attempt at a balance between health, social, and economic factors was evident throughout the experiences in the clinic patient room, walking through the community shantytowns, as well as in the board room of coalition groups fighting the AIDS epidemic. Nyumbani’s role is central to this fight, not just in Nairobi, but in Kenya and Africa as a whole. Its dedication to a multi-disciplinary service model is being replicated throughout the continent as one of the most effective methodologies to date.
Harm reduction is the non-judgmental and community-driven public health strategy used to address drug and chronic alcohol abuse by minimizing the harm associated with use of these substances. It is an important element of outreach programs directed at marginalized populations that include drug users and homeless chronic alcohol users. Though much work is still needed in mediating the health care needs of these vulnerable populations, unique efforts have been developed in Canada, United States and Brazil to facilitate the treatment of addiction, prevent transmission of HIV and hepatitis, and promote transition into long term care.

In the United States, the philosophy of harm reduction has had limited impact on health care provision evidenced by the federal ban on government funding for needle exchange programs lifted only two years ago. Despite this setback, a new approach that minimizes stigma associated with seeking treatment at methadone clinics, is the buprenorphine/naloxone formulation which can be dispensed in the office of American primary care physician. Physicians in Canada initiated shelter-based managed alcohol administration programs directed at chronic alcohol users who are homeless which has been shown to be effective at decreasing consumption and use of crisis services. While Brazil's government has been praised for its comprehensive approach to AIDS, it has been less responsive to act on the surging crack cocaine epidemic with harm reduction efforts preventing transmission of hepatitis directed at crack cocaine users being limited to the initiative of NGOs.

Harm reduction programs have been shown to reduce disease transmission, provide a means to access basic primary care, and help users transition into rehabilitation programs. The justification to support the documented public health benefits of these programs and counter what may be perceived as encouraging risky behaviors may require the medical community to re-visit primum non nocere, that is, first do no harm, and its extension to the principle of harm reduction.
Challenges to implementing an effective pediatric HIV treatment program when food security is not guaranteed: observations from Kibera

Food security, as defined by the World Health Organization (WHO), exists "when all people at all times have access to sufficient, safe, nutritious food to maintain a healthy and active life." This type of security is by no means guaranteed even in the world’s wealthiest nations, let alone in developing countries. Food insecurity is a reality for over 3.5 million individuals in Kenya—many of whom also face the reality of being HIV positive. The critical link between proper nutrition and adequate immune function is well established and must be a key consideration in the treatment of HIV. This is taken into account in the package of comprehensive HIV services offered by Nyumbani, a non-governmental organization (NGO) working with HIV positive children in Nairobi, Kenya. In the organization’s Kibera clinic alone, over 500 children are receiving HIV treatment services—including antiretroviral therapy (ART) and counseling, social and nutrition services. Nyumbani implements a nutritional program based on WHO guidelines for the treatment of severe acute malnutrition. This community-based approach allows for early detection and treatment of children with severe acute malnutrition in order to improve nutritional status and bolster the immune response. Despite such efforts, high rates of food insecurity and malnutrition in the community—coupled with decreasing levels of food aid—continue to pose a particularly intractable challenge to ensuring that HIV positive children thrive.
GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Clinical Experience and disease awareness in Gugulethu Clinic in Cape Town, South Africa

Gugulethu Community Health Center (CHC) is the main Primary care hospital for the township of Gugulethu in Cape Town, South Africa. Primary care hospitals have the most basic level of care, limited supplies and are common in the townships. There are secondary and tertiary level hospitals, which house specialists and perform surgeries. The payments for GC are based on income but this initial payment is very low and most of the services and medication provided are free of charge.

HIV is one of the most prevalent conditions seen in Cape Town. The percentage of HIV positive patients can be as high as 40% in the townships. Opportunistic diseases such as Tuberculosis is also a widely spread disease and is mostly seen in HIV positive patients due to their low CD4 count. Hypertension is one of the most common chronic diseases seen among the elderly mostly due to high salt, high fat diet and lack of exercise. Although they cannot be categorized as diseases, stabbing and gunshot wounds are seen commonly in the ER.

The Gugulethu Township is a mostly black populated area. Gugulethu is poverty stricken with unemployment rates as high as 60%. The Gugulethu CHC is the main hospital in this region and the patients are from the township itself. The main language spoken here is Xhosa.

In order to learn more about the patients’ lifestyle choices, a survey about patients’ point of view about their lifestyle choices and diseases was conducted. There were many challenges experienced by the patients as well as the providers seen at the hospital. Having non-Xhosa speaking doctors adds a challenge for them to understand the patient and for the patient to understand the advice given by the doctors. TB numbers are high in the population mainly because of the non-compliance. Even after the patient gets tested positive for TB, they might go home and not take any precautions to contain the condition there by spreading it. Teen pregnancy is also a very common occurrence in the Township because of the growing young adult population. The young mothers give birth at home, which prevents the administration of HIV drugs that can help contain the virus. Even with the challenges, the Gugulethu community overcome the barriers and provides the most appropriate care as possible.
GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Surveillance of Select Non-communicable Diseases in Rural Haiti

BACKGROUND

As the poorest country in the western hemisphere, Haiti has struggled with the surveillance of chronic non-communicable diseases such as diabetes, hypertension, cardiovascular disease, and renal failure. This struggle is especially apparent in the post-earthquake setting. Therefore, the purpose of this study is to evaluate the surveillance techniques used in the management of non-communicable diseases.

METHODS

Using the help of a translator, a questionnaire will be administered to patients seen in the primary care clinic associated with Project Medishare in the rural setting of Thomonde, Haiti. The target population will include those with hypertension, renal disease, diabetes, or cardiovascular disease. The questionnaire will inquire about the frequency of medical follow up visits, availability of prescription therapy, continuity of care, complications of disease resulting from inadequate treatment, as well as methods employed by the clinic to track chronic disease progression.

RESULTS

Results to date.

CONCLUSIONS

Results to date.
BACKGROUND
The Laikipia District of central Kenya is home to tens of thousands of indigenous peoples living in abject poverty. In the area surrounding Segera Mission alone there are approximately 12,000 individuals with little to no money, little access to clean water or sanitation, and unreliable transportation to the nearest hospital. Segera Mission is an organization that provides these services to the locals, including healthcare in their small clinic. Due to the conditions in the area, the clinic sees between 700-1300 patients in a given month, mainly due to diarrhea, parasites, and minor trauma. My aim was to assist in the clinic as well as to provide health education resources to the community.

METHODS
My main function while at the clinic was to assist the nursing staff with their daily needs. I triaged patients at house calls while the nurses attended the clinic, assisted in deliveries and procedures, took histories and physicals in the clinic, requisitioned and retrieved vaccinations from the District Hospital, and transported critically ill patients to the District Hospital. In addition to these roles, I also attempted to improve the overall public health in the communities. I traveled to villages and handed out chlorine tablets while engaging in a public dialogue about the importance of clean water. At the end of my project, I held a meeting with the elders of the various villages and held a daylong seminar on health issues including clean water, sanitation, nutrition, maternal-child health, and the dangers of indoor fires.

RESULTS
Over the course of my trip, I saw thousands of patients, administered hundreds of vaccinations, and assisted with nearly two-dozen deliveries in addition to advocating for patients and the community in various other ways. I dispensed chlorine tablets and taught several hundred people how to properly use them. I engaged the village elders in a conversation about improving the health of their respective communities and received positive feedback from individuals in the community as well as from the Mission.

CONCLUSION
My ten-week project in central Kenya was successful in that I achieved the goals I set out to achieve. Being able to assist in the community was a very fulfilling experience. Education and support can play a vital role in transforming the health of a community, and I did my best to provide that to a populace otherwise largely ignored.
Qualitative Assessment of Healthcare Challenges in Kenya

As a recipient of the Health Services Scholarship, I spent eight weeks volunteering in Kenya. Most of my time was spent working in the small Nairobi Hospital, but I also spent time at a larger hospital as well as volunteered at a medical camp in Northern Kenya. I gained clinical experience in both urban and rural environments. My time in Kenya provided me with an overview of healthcare challenges in Nairobi (such as accessibility, cost, etc.) as well as on the burden of non-communicable and communicable diseases.

The majority of my days were spent working with Dr. David Silverstein, an American cardiologist. A typical day at Nairobi Hospital meant my day began at 7am with a lecture on interpreting echocardiograms, followed by rounds in the wards, and finally I would assist Dr. Silverstein in his cardiology practice. Although I was getting little direct patient interaction at Nairobi Hospital, I learned about interpreting lab results and critical care as well as seeing how health care is delivered to upper and upper middle class populations in Nairobi. At Kenyatta, I witnessed overcrowded wards with sometimes multiple patients to a bed, and a healthcare system where access to drugs and laboratory tests and other diagnostic tools was extremely limited. Finally, my work in the temporary medical clinic in Maralal was very rewarding. We saw close to 700 patients in just three days. By the end of the first day, I was seeing my own patients and working with the physicians to discuss the diagnosis and treatment options. I struggled however with the fact that there was no follow-up and felt that at most what we were doing was just temporarily relieving pain, which would resume when the patients ran out of medications and no longer had a clinic or doctor to go to.
GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

A Midterm Survey to Determine the Efficacy of Tubaramure, A Program to Prevent Malnutrition in Children Under Two in Burundi

Tubaramure is a program, started in 2009, with the goal of reducing the occurrence of malnutrition in children under two years of age in two regions of Burundi, Ruyigi and Cankuzo. The program operates under a consortium of four nongovernmental organizations (NGO): Catholic Relief Services (CRS), Caritas, International Medical Corps (IMC), and Food for the Hungry (FH) and is financed by USAID. Each member of the consortium is charged with the implementation of one of the following three objectives:

1. Women and Children 0-59 months access quality nutrition and health services;
2. Households practice appropriate health and nutrition behaviors; and
3. Eligible women and children have increased intake of diverse foods.

IMC is charged with the first objective, and performs its work primarily through the training of medical personnel, and the delivery of equipment and supplies to medical centers. From June 20 to July 15 2011, a midterm survey was conducted to assess IMC’s role in Tubaramure and to determine if any changes should be made to increase its impact.

The survey targeted four groups of people: Head Doctors of each province and district (7), nurses and paramedics from 18 different health centers (36), community health worker focus groups (8), and beneficiary focus groups (6). The majority of questions used were open questions which allowed for multiple responses. Other questions were closed questions, also allowing for multiple responses, and yes/no questions.

The main results show that while Tubaramure has so far been effective in reducing malnutrition and improving health, its effects may not be sustainable. Also, the goal of IMC to train health care workers in various domains related to child health has not been very effective as a majority of those trained were not able to answer technical questions related to their training.

Recommendations include a closer partnership with the Ministry of Health in order to improve the chances of the program’s sustainability, more trainings for health care workers, and more frequent observations of health care workers.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Healthcare Experience in Jaipur, India

Mahatma Gandhi Hospital is the closest accessible hospital for over 1,000 people living in rural villages surrounding Jaipur city, in Northern India. A large majority of individuals living in these communities face serious healthcare challenges including malnutrition, limited access to clean drinking water, and inadequate access to health education. Due to the shortage of preventive health care, patients present to the hospital and the local clinics with advanced stages of disease. My goal was to experience the workings of a medical system in a resource poor setting.

The internship lasted eight weeks, during which I split my time between a community health rotation with medical students and shadowing in various departments throughout the hospital. During my community medicine rotation, I visited several local clinics, including an Aaganwari Center devoted to the improvement of women and children's health and a Direct Observation Treatment Strategy (DOTS) Center for tuberculosis patients. For the remainder of my time, I shadowed residents and physicians in Pediatrics, NICU, General Surgery Clinic, General Medicine, and the Emergency ward. By the end of my stay, I had observed numerous deliveries, a laparoscopic gall bladder removal, and an appendectomy. Additionally, I learned how to perform a newborn exam in the NICU and deliver immunizations. While aspects of the Indian medical system are vastly different from that of the United States, the general practice of medicine remains the same.
GLOBAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Understanding the Management and Treatment of HIV in Kenyan Children

There is an estimated 1.5 million people living with HIV in Kenya, many of whom are Kenyan children. This astounding statistic is in large part due to high birth rates, lack of access to medical care, prolonged breast feeding and high rates of maternal infection. While volunteering at the Lea Toto clinic in Nairobi, Kenya for six weeks, I managed the care of children with HIV. I learned how to conduct a physical exam specific to HIV-positive patients, draw blood and make adjustments to their anti-retroviral therapy (ART) regimens. In addition, I was able to work in the slums alongside social workers and community health workers to assess how the problems of adherence to ART medication and the social stigma associated with having HIV affected the children's health and development. At the end of my experience abroad, I conducted a literature review exploring both the incidence of HIV/AIDS in Africa and the specific public health initiatives that are currently in place to slow its progression in Kenya. Working at the Lea Toto clinic gave me an opportunity to provide HIV-positive children with medical, nutritional, social and psychological support and it has reaffirmed my future desires to provide healthcare to underserved populations around the world.
The use of ayahuasca among the Kichwa of Ecuador: The potential dangers of mixing western pharmacotherapy and traditional shamanistic medicine

Ayahuasca [aja’waska] is a hallucinogenic beverage that is made with two indigenous plants of the Northwest Amazon region, especially by the Kichwa tribe of Ecuador. Shamans in these regions have used this drink for centuries claiming its diagnostic and curing effects, as well as its psychedelic effects being a route to the supernatural realm. Shamans of the community are very knowledgeable in its usage as well as other medicinal plants of the Amazon; however, until recently, Western medicine was not readily available. With the recent construction of a road connecting the community to other small communities and the river launch point to the city, there are concerns of the potential blending of modern pharmacotherapy with traditional medicinal plants such as Ayahuasca.

Studies of this brew have isolated its active substances and derivates, two of which are N,N-dimethyltryptamine (DMT) and a plant alkaloid from the β-carbolines. DMT is a natural psychoactive indolealkylamine, a non-selective serotonin 5HT agonist. It has a high affinity for serotonin 5HT1A receptors, while the active metabolite bufotenine has higher affinity for 5HT2A. The active metabolite occurs as a result of metabolism by the cytochrome P450 system CYP2D6. DMT is mainly inactivated through the deamination pathway mediated by monoamine oxidase-A (MAO-A). β-carboline alkaloid is a well known potent MAO-A inhibitor. Thus, when dually ingested in the Ayahuasca drink, a β-carboline such as harmaline inhibits the breakdown of DMT and increases the synaptic levels of the active metabolite, bufotenine.

After spending several days with the very small and isolated Kichwa community in the Napo region of Ecuador, I realize how mixing traditional shamanistic medicine and western pharmacotherapy could lead to potentially fatal consequences. The improved access to Western medical care for the Kichwa people and the influx of Western tourists, students, and volunteers, poses a great risk of mixing the use of Ayahuasca with their current pharmacotherapy. Common drug interactions of concern are selective serotonin reuptake inhibitors (SSRIs) among others. This class of drugs is commonly prescribed in the Western World and when taken with Ayahuasca can cause a toxic increase in serotonin causing serotonin syndrome. 2 Serotonin toxicity is an adverse drug reaction that can have mild to life threatening symptoms caused by increased serotonergic activity. The classic clinical description includes changes in mental status, autonomic hyperactivity, and neuromuscular abnormalities. However, symptoms can range from diarrhea, tremor, myoclonus, dilated pupils, hyperthermia, and increased blood pressure and heart rate that may eventually lead to metabolic acidosis and shock. It is often difficult to diagnose because of the range of severity of the symptoms.

After speaking with a Kichwa shaman, it was very clear that he was unaware of any interactions or adverse reactions that could occur with Ayahuasca or any other medicinal plant therapy because he was never exposed to such Western pharmacotherapy before. Therefore, it is in my opinion that shamans of the indigenous communities in the Napo region of the Amazon receive some education about pharmacotherapy of the modern world and about fusing the indigenous shamanistic medicine with modern western medicine. It is also important that travelers and physicians treating those who may be traveling to indigenous communities be made aware of the potential risks including drug-drug interactions before taking Ayahuasca or other medicinal plants.
Global Health

School of Medicine and Health Sciences

Observation and Assessment of Maternal Healthcare in Arusha, Tanzania

The United Nations identified “Improve Maternal Health” as goal five of the eight Millennium Development Goals, aiming to reduce maternal mortality by three quarters from the years 1990 to 2015. Over 90% of maternal deaths occur in developing countries, and because most of these deaths are largely preventable, it is a major concern in the area of global health. Tanzania is one of the top ten countries for highest maternal mortality rates - more than three times the world average. My time in Arusha, Tanzania this summer allowed me to observe healthcare practices surrounding birth to identify factors that contribute to bad outcomes in maternal/fetal health.

While Arusha is home to a large, relatively well equipped, 450-bed facility (Mt. Meru Regional Hospital), routine maternal/fetal health for the residents of Arusha is provided at council run clinics. This summer, I worked for one of the smaller clinics in Arusha, called Ngarenaro. Under the supervision of Dr. Japhet Kivuyo, Ngarenaro is a USAID-supported clinic that provides reproductive health and pediatric services for more than 200,000 Tanzanians. Here I was able to observe antenatal care (including Prevention of Mother to Child Transmission services), labor and delivery, preventive care for children under the age of five, family planning services, and acute care for both child and adult outpatients.

The practices at Ngarenaro were superior to what I had envisioned, with high rates of women receiving three prenatal exams, great success in the prevention of mother-to-child HIV transmission, and decent postnatal follow-up care. However, there are still many women who do not come to the clinic for their deliveries. The prenatal care included patient education, but it lacked information on planning for the delivery, and because husbands were largely not present for these visits, the importance of getting to the clinic in time for delivery was not communicated adequately. Another obstacle in quality of care was limited electricity, due to power rationing in Tanzania. The clinic was unable to perform Caesarian sections and lacked any modern monitoring technology. A literature review will be completed to assess how the difficulties observed at Ngarenaro align with the greatest contributors to bad outcomes in maternal health, and identify measures that can be taken to improve care at Ngarenaro and similar clinics in Tanzania.
A Systematic Review and Meta-analysis of Peroneal Artery Perforators for Free-Tissue Transfer and Local Flaps

BACKGROUND

The aim of this study was to evaluate the available literature on the density and location of peroneal artery perforators in the lower leg for the application of free tissue transfer. Several analytic methods have identified perforators in the setting of fibula osteocutaneous flaps utilizing cadaveric, anatomic and clinical models; however, there has been no true consensus on the optimal fibula interval to reliably capture these perforators for flap and skin paddle design.

METHODS

A systematic review of the MEDLINE and Cochrane databases was performed to identify all anatomic, clinical and radiographic reports of the locations of peroneal artery perforators in the lower leg. English language studies that detailed complete perforator anatomy in relation to the fibula along a longitudinal or midaxial line were included. Abstracts were reviewed, and an additional bibliographic search was performed to capture all pertinent documents. The locations of perforators were indexed along tenths of the total fibula length to incorporate a uniform format. Perforators were grouped by interval, and a subgroup comparison of musculocutaneous (MC) and septocutaneous (SC) perforators was performed. Key words included “fibula/ or fibula flap”, “peroneal artery”, “leg/ lower leg” and “perforator”.

RESULTS

A total of 9 preliminary documents fitting the inclusion criteria were reviewed. These studies represented 3 clinical and 6 cadaveric reports, for a total raw analysis of 392 legs and 1,626 peroneal perforators. Of these, 8 studies listed combined MC and SC data, with subgroup distribution available in 7. 1 study included only SC data, and was therefore utilized in only the SC subgroup analysis.

CONCLUSION

The systematic review and meta-analysis of all available and complete peroneal artery perforator data demonstrates a predominate density over the 0.6 interval of the lateral leg. This interval should be considered during flap design and elevation to reliably capture irrigating perforators for free and local flap applications.
Disaster Preparedness—Formalizing a Comparative Advantage for the Department of Defense in U.S. Global Health and Foreign Policy

BACKGROUND
Disaster preparedness is a comparative advantage of the Department of Defense (DoD) in the global health arena. It is in line with the domestic interest of sustaining foreign natural disaster assistance and the foreign policy interest of maintaining national security.

METHODS/RESULTS
The DoD humanitarian assistance policy guidance published in 2009 states Disaster Preparedness should be considered as a key priority in humanitarian assistance engagement. Unfortunately, a whole of government disaster preparedness program framework does not exist to facilitate effective and efficient implementation. Leveraging the United Nations Hyogo Framework for Action agreed upon by 168 nations to take action and reduce disaster risk by 2015, the DoD could synchronize disaster preparedness efforts with other interagency and international partners.

CONCLUSIONS
Increased civilian–military cooperation in disaster risk reduction supports the whole of government approach to work in a more coherent manner in pursuit of shared foreign policy goals. It also maximizes the ability to deliver critical national capacity in the health sector and beyond. Disaster preparedness is an essential element of U.S. global health and foreign policy, and the DoD must be a critical partner in a whole of government approach.
Maternal Healthcare in Ecuador

Maternal mortality is one of the most preventable causes of death in the world, and it exemplifies one of the most unacceptable gaps between the developed and developing countries. With an underestimate of 159 cases of maternal mortality per 100,000 children born, Ecuador is no exception to this rule. A different discrepancy is elucidated when maternal healthcare in the public and private healthcare systems are compared, as most of these deaths occur in public healthcare settings. During my time in Ecuador I assessed the four tiers of the Ecuadorian health care system, with an emphasis on women’s health care and prenatal care.

Throughout my rotations in the tiers of the Ecuadorian health care system, I collected information regarding the length patient visits, the assessments that were done on the patients, as well as stories that were unique to each experience. Not surprisingly I found that more time and resources were spent on those who could afford private health than to those who utilized the public healthcare system. Additionally the public health care system often dealt with more life threatening emergencies than private facilities which, aggravated by the lack of resources available to the clinics, often led to unfortunate outcomes.

Ecuador has striven to reduce obstetric emergencies in many ways. In an effort to promote a healthy life-style and decrease the number of emergency visits, Ecuadorian public hospitals have initiated community outreach programs to reach out to those living in remote areas. These programs varied in topic from the importance of daily hygiene to contraceptive use and prenatal care. However these programs have not stopped the rate of complications during pregnancy from rising further. More recently there has been a push in Ecuador to improve access to prenatal care, which is no small feat considering one third of the country consists of the Amazon Rainforest. However these strides are making a huge impact in local communities as women are able to newly built clinics faster, decreasing maternal complications that are irreversible upon arrival.

My experience in the Ecuadorian clinics has provided me with stories unique to the different experiences I had in each healthcare setting. It was truly one that could not be replicated in a different setting, and it exposed me to many unique circumstances which ultimately gave me a better understanding of prenatal care in a third world country.
Neurosurgery is the surgical discipline focused on treating those central, peripheral nervous system and spinal column diseases amenable to mechanical intervention.

According to the U.S. Accreditation Council of Graduate Medical Education (ACGME), “Neurological Surgery is a discipline of medicine and that specialty of surgery which provides the operative and nonoperative management (i.e., prevention, diagnosis, evaluation, treatment, critical care, and rehabilitation) of disorders of the central, peripheral, and autonomic nervous systems, including their supporting structures and vascular supply; the evaluation and treatment of pathological processes that modify the function or activity of the nervous system, including the hypophysis; and the operative and nonoperative management of pain. As such, neurological surgery encompasses the surgical, nonsurgical and stereotactic radiosurgical treatment of adult and pediatric patients with disorders of the nervous system: disorders of the brain, meninges, skull base, and their blood supply, including the surgical and endovascular treatment of disorders of the intracranial and extracranial vasculature supplying the brain and spinal cord; disorders of the pituitary gland; disorders of the spinal cord, meninges, and vertebral column, including those that may require treatment by heat fixation, instrumentation, or endovascular techniques; and disorders of the cranial and spinal nerves throughout their distribution.”

Neurosurgery is commonly referred to as “Brain surgery,” much like rocket science is used to refer to a task requiring significant knowledge and skill. Therefore, neurosurgery is usually a misunderstood field. Neurosurgery is not all glamorous, but it is also not all too bad. Hopefully, this project will help illustrate the various neurosurgical fields across the globe and will be an educational experience for many individuals not involved in the neurosurgery.

The project’s objective is to inform the general public about the various neurosurgical tools/equipments available, the lifestyle of these neurosurgeons, and the different techniques used to tackle neurosurgical issues like tumor removal in 17 different countries, from Germany to India to Japan to Australia and more.
SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Opportunities and Challenges in Undertaking a Descriptive Analysis of Washington D.C.’s Gay, Lesbian, Bisexual and Transgender Community

BACKGROUND

Despite the presence of a large number of GLBT residents in the D.C. area, little action has been taken in the past to comprehensively describe this population. The dearth of information impacts the ability of the Mayor’s Office of GLBT Affairs to attain a complete understanding of its constituents. The objective of this study was to identify the opportunities and challenges inherent to comprehensively describing Washington D.C.’s GLBT population in order to assist the Mayor’s Office in advocacy and policymaking.

METHODS

Qualitative methods were used to evaluate the work of Mayoral Liaison Offices in jurisdictions including San Francisco, Chicago, New York, Philadelphia and Toronto, in addition to a comprehensive assessment of the information being collected on D.C.’s GLBT residents by local government agencies, non-profits, academic institutions and other organizations. Data was produced from phone and email conversations, brief surveys, comprehensive Internet research and consultations with issue experts. The data collected was organized according to agency and topic area to provide a clear illustration of the current level of information and major gaps therein. The analysis of this data focused on the extent of GLBT-specific information currently collected as well as data collection practices and methods of information storage and organization by relevant agencies and actors.

RESULTS

There are substantial limitations in the collection of standardized data describing Washington D.C.’s GLBT residents. Specifically, GLBT issues are of low priority within D.C.’s government agencies, issues of privacy and sensitivity are not being addressed, GLB and T issues are currently amalgamated, there is a lack of data on persons who do not fall into special sub-populations, a lack of resources to utilize or analyze data that is currently available, and no centralized place for recources or platform for collaboration.

CONCLUSIONS

The demonstrated limitations in data collection, together with a lack of resources, issues regarding privacy and sensitivity, and absence of strong leadership at the city and federal level, impact the visibility of D.C.’s GLBT community to policymakers. Given the high value placed on descriptive data in policymaking, D.C.’s GLBT residents are disenfranchised. Ten recommendations were provided to guide the Mayor’s Office of GLBT Affairs in efforts to undertake a descriptive analysis of its constituency. Key amongst these were recommendations to convene an advisory group to consult on the analysis, develop a platform for storing and sharing descriptive data on the GLBT community, and establishing District-wide data collection standards, particularly for demographic information.
Mandatory Influenza Vaccination of Healthcare Workers

The effects of seasonal influenza, measured in terms of morbidity, mortality, and loss of productivity is a serious public health concern. According to the Centers for Disease Control and Prevention (CDC), on average, seasonal influenza is responsible for more than 200,000 hospitalizations and 36,000 deaths each year. The Advisory Committee on Immunization Practices (ACIP) first recommended annual influenza vaccination programs for healthcare workers (HCW) in 1981. Despite recommendations by the CDC, only an estimated 42% of HCWs get vaccinated annually. Clinical studies have shown that HCWs vaccinated against seasonal influenza significantly improve the health of the worker and of the patient, as well as help reduce costs associated with influenza morbidity and mortality. In 2011, I took part of a research study that reviewed the legal environment surrounding influenza vaccination among the healthcare workforce. The study was performed under the supervision of Alexandra M. Stewart, JD, Principal Investigator and Assistant Professor at The George Washington University School of Public Health and Health Services. As a legal research assistant, I identified and charted the duties prescribed under the laws, reviewed the statutory duties against a set of six elements, developed detailed tables that outlined the legal status of each state and helped draft a comprehensive literature review and model law. The research showed that 19 states (AL, AK, CA, IL, KY, ME, MD, MA, NH, NY, NC, OK, PA, RI, SC, TN, TX, UT, and VA) and the District of Columbia have enacted laws that require health care employers to develop and implement influenza vaccination programs. Although not all jurisdictions met the six elements of a comprehensive mandatory vaccination law, the results of this study suggest a growing movement of states implementing mandatory HCW influenza vaccination programs.
Can private insurance companies leverage ACA mandated coverage requirements for contraceptives to reduce plan costs and address the Healthy People 2020 goal to reduce unintended pregnancies? 

Many health plans and employers have comprehensive wellness programs; however, family planning and contraceptive use is not approached strategically. A review using analysis from existing studies of unintended pregnancy rates, cost-effectiveness of long acting reversible contraceptives (LARCs), the association between noncompliant contraceptive use and unintended pregnancy, long-term costs of unintended pregnancy versus cost of LARCs, as well as insurance provider approaches to covering LARCs was undertaken. Challenges for increasing LARC use LARCs include social acceptability, prescriber and insurer propensity towards oral contraceptives, lack of incentives for encouraging LARCs. Options considered: 1) Comply with ACA provisions without making effort towards providing additional family planning services; 2) Implement incentive programs encouraging comprehensive family planning counseling that encourages use of LARCs; 3) Review billing processes including outreach to providers to become in-network providers as well as creating bills that keep family planning services confidential. Options were considered using three criteria: social acceptability, cost-effectiveness, and administrative feasibility.

LARCs offer a cost-effective approach to reducing unintended pregnancy; they are underused because of social acceptability and high upfront costs. Women of childbearing age, providers, and payers are stakeholders affected. Implications of encouraging LARC use: higher compliance, lower prescribing costs (by avoiding high cost branded oral contraceptives), and lowered costs associated with unintended pregnancy. Provider training is essential to ensure providers understand LARCs are safe.
Beyond Flexner: A Literature Review of the Social Mission of Medical Education in the 21st Century

PURPOSE

In 1910, the Carnegie Foundation published Medical Education in the United States and Canada, by Abraham Flexner subsequently known as the Flexner Report. This document catalyzed enormous and important changes in medical education in the United States that continues to significantly influence current methods of training. At a point in time in which we celebrate the 100-year legacy of the report, we also evaluate its unintended shortcomings in relation to our current state of medical education. More specifically, how do existing models address or ignore the social mission of medical education. Part of this analysis includes identifying the existing evidentiary base of literature that promotes socially accountable medical education. A review of literature was performed to answer the crucial question, how do medical schools demonstrate social accountability? Eight modalities of social accountability were identified by an advisory committee and a literature review was conducted for each modality. Methods: The authors searched relevant literature pertaining to the eight modalities using the following databases: Pubmed, Medline, CINAHL, and Google Scholar. Bibliographies from selected articles were searched as well as references from relevant websites (ex. AAMC). Articles were considered relevant if they included keywords, fit into the modality scope, and included one or more of the three social mission components. Results: In general regards to all of the modalities, extensive literature exists involving components of each modality that influence students to enter primary care. A significant literature base exists for components that encourage students to work in underserved areas. Literature evaluating components that enhance underrepresented minorities in medicine is not as consistent or as clearly delineated across all modalities. Overall, specific up to date strategies are lacking for Pipeline programs, Financial Management, Mentorship, and Post-Graduate Engagement.

DISCUSSION

The current literature broadly describes various approaches to promoting social mission within medical education. The modalities chosen made it feasible to categorize these ideas and easily search for recurring themes. Within each modality, simple recommendations could be generated for schools that wish to enhance their social accountability and transparency. However, the modalities also highlighted the paucity of data in several key areas. While many strategies likely exist to encourage students to pursue primary care and practice in underserved areas, much of this may be informal or not well studied. A review such as this can serve the purpose of sharing evidenced based strategies that medical schools use to propagate values of social accountability and graduate socially accountable physicians.
Comparison of Mystery Caller Methodology to Direct Calls to Evaluate Access to Care After an Emergency Department Visit

BACKGROUND
The mystery caller methodology has been used in a number of health services research studies to evaluate access to care. In 2011, the Department of Health and Human Services funded a nationwide mystery caller study to assess rates of access to care. Upon public release of information about the study, the funding was rescinded due to widespread discontent, mainly by physicians. Dissenters complained that the study was deceptive and similar information could be obtained by direct query of providers about appointment availability.

Objectives: The objective of the study was to compare appointment success rates and wait times using the mystery caller and direct caller methodologies. We hypothesized that the direct call approach would overestimate appointment availability as compared to the mystery caller approach.

METHODS
The mystery caller scenario calls were made by trained research assistants posing as hypothetical patients requesting an appointment for hypertension followup after an ED visit. The direct calls were made by a GW research assistant asking about appointment availability based on insurance status. We compared success rates and average wait times for patients with private insurance using bivariate analysis (one sided t test). We also compared agreement for appointment success rate by the two approaches for individual clinics using a kappa statistic.

RESULTS
Of a total of 31 private clinics, 50.6% of patients could secure an appointment with the mystery caller private patient scenario as compared to 64.5% with the direct call approach (p=0.15). Kappa for success rate by individual clinic was 0.72. Average wait time using the hypothetical call approach was 10.1 days (95% CI 5.7,14.5) as compared to the direct call approach wait time of 16.4 days (10.1,22.7).

CONCLUSION
The direct call approach did have a higher appointment success rate than the hypothetical caller approach, though results were not statistically significantly different, likely due to the small sample size. Agreement was fairly high by individual provider of 0.72.
Inadequate access to medical services is a well-known problem and triggered the Patient Affordable Care Act. Millions of Americans insured or not, struggle to access physicians. Medicaid users have a particular problem due to the lower reimbursement rates offered by Medicaid compared to other insurers. In 2009, DC adopted a policy raising Medicaid reimbursement to be on par with Medicare.

OBJECTIVES

This study aims to understand whether outcomes, particularly success in obtaining follow-up care, have changed for Medicaid fee-for-service patients (and others) in DC in comparison to the years before the act was introduced in 2009. Washington, DC, is one of the first areas with Medicaid parity and this in conjunction with a highly insured population, makes DC an instructive model for the country when legislation goes into effect nationwide. Therefore, this study has potential long-term implications indicating what the future may hold when the Patient Affordable Care Act (ACA) goes into effect.

METHODS

First, a number of clinics were randomly identified across Washington, DC. Scripted calls were made to these clinics simulating a 40 year old patient needing follow-up care after being recently discharged from the ER to monitor his/her hypertension. Script scenarios were varied based on patient insurance status and clinic type. Out of a total of 66 provider calls completed, 31 calls were completed to private providers (Medicaid, private, uninsured and Medicare scenarios) and 35 calls to safety net clinics (uninsured, Medicaid and DC Alliance safety net scenarios). Data from each scenario was cross analyzed and compared using Chi-Square analysis.

RESULTS

Calls made as Medicaid fee-for-service patients seeking care at private providers faced the most challenges with only 30.8% success, compared to 58.1% for privately insured patients (p= 0.04). Overall declines in success rates were also noted compared to previous studies from 2005 and 2008. The reimbursement policy changes did not affect Medicaid fee-for-service patients’ success in obtaining follow-up care.

CONCLUSIONS

Access to care has not improved in the nation’s capital despite a highly insured population and recent legislation. Policy changes have not led to the expected access improvements for the Medicaid fee for service patients. Several reasons may contribute to these findings, including providers who are uninformed of changes, which should be further explored.
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SCHOOL OF MEDICINE AND HEALTH SCIENCES
Implementing FrontLine SMS Technology to Improve Disease Surveillance System in Hubli, Karnataka, India

BACKGROUND
The Integrated Disease Surveillance Project (IDSP) is a World Bank funded program to assist the Government of India in improving the state-based disease surveillance systems. The basic public health structure in Karnataka State consists of State Hospitals, District Hospitals, Primary Health Centers (PHC), and village-level Sub-centers (SC). Each District Hospital is affiliated with a number of PHCs that serve a population of approximately 30,000 people. Each PHC is affiliated with approximately 6 village SCs which monitor a population of approximately 5,000 each. Under the IDSP Program, there is a system for weekly reporting using Forms S, P, L, and W. The SCs (each associated with a population of 5000) create weekly documents (Form S) containing information on all seasonal diseases reported by the field workers. Form S is taken by foot from each of the 6 village SCs to the PHC where the information is tabulated into a single document (Form P). Form P is then electronically sent (via email) to the District Health Office to take appropriate containment measures.

My project was aimed at improving the communication between the SCs and PHCs by replacing the manual delivery of Form S with a digital delivery system using a text message based electronic forms software called FrontlineSMS. Such a system would help deliver a report in the event of a serious outbreak within minutes to a Medical Officer at a PHC to take immediate containment measures.

METHODS
I selected a PHC in the town of “Byahatti” located in the Hubli/Dharwad District to install the FrontlineSMS Software. In addition, I chose 4 SCs associated with the Byahatti PHC, and distributed one mobile phone to a nurse managing each of the SCs. Following the distribution of the mobile phones and the software setup, I trained the Chief Medical Officer at the PHC and the nurses at the SCs on how to use the FrontlineSMS both on the computer as well as the mobile phones. I created an electronic Form S which could be sent from the mobile phones to the computer at the PHC using FrontlineSMS.

RESULTS
The District Surveillance Officer (DSO) at the Hubli/Dharwad District Health Office agreed to pilot this system for one year to assess its effectiveness for future adoption at other PHCs and SCs in Karnataka State.

CONCLUSIONS
All conclusions and results will be provided at the end of summer 2012.
Access to Urgent Pediatric Primary Care Appointments in the District of Columbia

BACKGROUND

Timely access to acute primary care appointments after an emergency department (ED) visit has become a challenge for both providers and patients. Previous studies have documented disparities in accessing adult primary care and pediatric specialty care, especially among those lacking private insurance. There is little data regarding urgent pediatric primary care access. Concerns over pediatric provider access need to be addressed as public and private insurance expansions begin within health reform.

OBJECTIVE

This study measured pediatric access to urgent primary care appointments within the District of Columbia (D.C.) following an ED visit. We hypothesized there would be a disparity in access for uninsured children or those with Medicaid.

METHODS

We used mystery caller methodology to evaluate rates of appointment access for pediatric patients. Calls were made to randomly selected private pediatric practices as well as pediatricians at safety net clinics. Research assistants posed as a parent calling to secure an urgent appointment for their child following a recent ED visit for urinary tract infection symptoms using a standardized clinical script that varied by insurance status. We calculated rates of appointment success as well as average length of time between call date and appointment date. All appointments were canceled prior to termination of the call. We analyzed differences in appointment success rates and wait times using bivariate chi2 analysis.

RESULTS

We sampled 57 safety net clinics and 29 private clinics. Although the results were not statistically significant (p=0.55), successful appointment rates were the lowest among Medicaid (27.8%) callers attempting to make appointments at private clinics. Calls made to safety net providers for the Medicaid patient scenario (48.8%, p=0.38) or uninsured patient scenario (47.7%, p=0.42) had the highest appointment success rate however had longer wait times. The average appointment wait time at safety net clinics for Medicaid patients was 12.3 days (95% CI, 3.5 to 21.1) and 10.4 days (95% CI, 6.7 to 14.1) for uninsured patients. Average appointment wait times for private patients at private practices were 1.9 days (95% CI, 1.0 to 2.7).

CONCLUSION

This study did document a disparity in access to urgent pediatric primary care appointments between callers with different types of health insurance in D.C. Although appointment success rates were not different by practice setting or insurance type, average appointment wait times were significantly longer for callers to safety net providers than private practices. Public policies that improve the capacity of pediatric safety net providers and clinics are necessary to improve access.
The Economics of Health Care Across OECD Countries

This paper looks at the relationship between healthcare spending per capita in OECD countries and respective patient outcomes, which is measured on a mortality/incidence (M/I) basis looking at many illnesses common across OECD countries. OECD countries are used in the analysis of patient outcomes across countries in order to compare the US to countries with similar economies, societies, and government policy. Additionally, the data on healthcare spending in these countries is most readily available as are the incidence and mortality rates from most illnesses. This paper uses empirical data to draw conclusions regarding the efficiency of the US healthcare system with respect to various other systems around the world. Past research has shown that the US has better patient outcomes across various illnesses; however this paper looks to tie the marginal increase in patient outcomes to a cost which is likely to be disproportionately high.
HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Delayed Access to Nutrients After Exercise Results in Reduced Mean Glucose Concentration for 15h Post Exercise in Young Men with a Family History of Type 2 Diabetes

OBJECTIVE

To study differential glucose responses when young men with a family history of Type 2 diabetes consume a carbohydrate/protein beverage either immediately or 3h after a 40min resistance exercise bout.

METHODS

In this cross-over study, male participants (n=7; 23 ± 3 years, BMI=23 ± 3) underwent two 48-h stays in a whole-room calorimeter. The first 24-h served as a control day. On the second day participants completed a 40-min resistance exercise protocol and consumed 600g of 1% chocolate milk (400 kcal; 6g fat; 66g carbohydrate; 21g protein) either immediately after the bout (IPEN) or 3-h after completing resistance exercise (3h-PEN). Blood glucose concentration was measured throughout the 48h period using a continuous glucose monitoring system, and energy expenditure during the exercise bout was measured with whole-room indirect calorimetry. We calculated the mean blood glucose concentration starting when participants finished the exercise through release from the study 15h later.

RESULTS

Mean post-exercise blood glucose was significantly lower following the 3h-PEN condition (93 ± 9 mg/dL) when compared with the IPEN condition (100 ± 7 mg/dL; P=.04). Mean energy expenditure during the resistance exercise bout was not different between IPEN (197 ± 19 kcal) and 3h-PEN (193 ± 43 kcal; P=0.8), confirming that the effort of exercise was fairly consistent during both experiments.

CONCLUSIONS

These preliminary results indicate that delaying nutrient ingestion after resistance exercise may promote significantly lower mean glucose in young men with a family history of diabetes, when compared with immediate post-exercise nutrient intake. A larger study to confirm this finding is warranted. This study was funded by the GW Department of Exercise Science and the United States Department of Agriculture Beltsville Human Nutrition Research Center.
HEALTH SCIENCES

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

A PMR and PCMR Analysis of Radiation and Mesothelioma in the United States Transuranium and Uranium Registries

BACKGROUND

Mesothelioma has been associated with therapeutic radiation. This study examines the relationship between occupational radiation and excess deaths from mesothelioma among former nuclear workers.

METHODS

Proportionate Mortality Ratio (PMR) and Proportionate Cancer Mortality Ratio (PCMR) analyses were performed using the NIOSH Life Table Analysis System. Univariate analysis was performed utilizing SAS 9.1 software.

RESULTS

A PMR of 62.40 (p<0.01) and a PCMR of 46.92 (p<0.05) were found for mesothelioma. PMRs for the four external radiation quartiles were 61.83, 57.43, 74.46, 83.31. PCMRs were 36.16, 47.07, 50.31, 69.43. The PMR and PCMR for trachea, bronchus, and lung cancer were not significantly elevated (p>0.05).

CONCLUSIONS

The exposure response relationship between cumulative external radiation and the PMR and PCMR for mesothelioma suggest that external radiation is associated with an increased risk of mesothelioma. The lack of a significantly elevated PMR and PCMR for trachea, bronchus, and lung cancer suggest that asbestos did not confound this relationship.
Clinical Presentations at Two Disaster Medical Assistance Team Sites Post Hurricanes Gustav and Ike—Louisiana and Texas, 2008

BACKGROUND
In the aftermath of a natural disaster, the risk of injury and illness is often increased due to unsafe or unsanitary conditions and environmental hazards. Analyzing clinical data from electronic medical records (EMR) can provide valuable insight concerning the health consequences communities experience after an emergency.

OBJECTIVE
To conduct a literature review identifying the methods by which post-hurricane morbidity is analyzed, as well as which clinical presentations are most prevalent in the wake of a domestic hurricane. Additionally, EMR from the National Disaster Medical System (NDMS) will be analyzed to determine which clinical conditions were most frequently seen at Disaster Medical Assistance Team (DMAT) sites during the 2008 hurricane season. The relative frequencies of clinical presentations at each site will also be compared to determine whether they varied by location, gender, or age. Methods: Literature review and retrospective descriptive analysis using EMR.

RESULTS TO DATE
Morbidity data was published in 21 peer-reviewed journals and official reports. The most common chief complaints after domestic hurricanes included wounds, upper respiratory disease symptoms, lacerations, musculoskeletal issues, shortness of breath or cough, gastrointestinal problems, and cardiovascular disease. The top diagnoses included: medication refills, wound care, supplies, skin/wound infections, and respiratory infection/disease. To date, data analysis has not been conducted using EMR data to examine the clinical presentations of patients seen at DMAT sites post Hurricanes Gustav and Ike.

CONCLUSIONS
Retrospective analysis of EMR can identify common clinical presentations in the aftermath of a disaster. Understanding the health consequences of hurricanes can lead to better preparedness procedures and policies, thus improving the health outcomes of vulnerable populations who are likely to be affected by future hurricanes.
Impact of Network of Maharashtra By People Living With HIV (NMP+) in Helping HIV Positive Women Meet Their Needs

Network of Maharashtra By People Living With HIV (NMP+) is an NGO based in the State of Maharashtra, India and they have their office in the city of Pune. The organization has several programs set up throughout the state and throughout the city of Pune to provide cares to people living with HIV. This study tries to examine the impact of NMP+ on the women they serve. The expected outcome was that the longer a woman was involved with NMP+ or the more active her role, the better able the woman and her family is to meet her physical, daily, and psychological needs. Through one of their established programs titled Children Affected by HIV/AIDS (CHAHA), eleven HIV positive women were interviewed as well as six of the employed Outreach Workers. Their involvement was considered with respects to the CHAHA program and all the data was obtained through in-depth interviews conducted with the assistance of a translator. The results were inconclusive partially because of the lack of family support the majority of these women had and because the main priority of these women was survival. It was found that the CHAHA program simply helped in a general sense with primary financial needs for the household and education and emotional support. As a recommendation, the CHAHA program and NMP+ should if possible provide more financial aid to families based on individual household situations (amount of income, number of children, etc) and provide more for the education of these children such as tuition and extra study aid. Future research could be geared towards the impact of such NGOs on children and support in an emotional sense.
Application of Vibration Doppler Imaging in the Differentiation of Lesions in a Phantom Simulation

PURPOSE

The purpose of this study was to investigate the use of vibration Doppler imaging to differentiate lesions of varying composition.

MATERIALS AND METHODS

We constructed a tissue mimicking phantom into which we inserted objects of different consistencies to mimic lesions in liver tissue. To simulate a variety of lesions we used a pistachio without its shell, a pistachio with its shell, an olive, an olive seed, a seedless grape and a grape with a seed. We used a 7 MHz transducer and the vascular presets on a Phillips IU22 Ultrasound machine. The images were obtained in 4 sets namely: B-mode imaging, B-mode plus Power Doppler without vibration, Power Doppler with manual vibration (tapping on the container) and finally B-mode plus Power Doppler with higher frequency steady mechanical vibration (placing a phone vibrating at a constant frequency on top of the phantom).

RESULTS

We found that applying manual vibration to our simulated masses gave better definition to the borders of the “lesions” when compared to the images in plain B-mode imaging alone. Border definitions further improved when the higher frequency constant vibratory waves emitted from the cell phone were applied. With the higher frequency vibratory waves we were also able to better distinguish the internal textures of the “lesions” in comparison to both the plain B-mode imaging alone and when B-mode imaging was coupled with Power Doppler and manual vibration.

CONCLUSION

Vibration Doppler imaging improves the border definitions and internal textures of lesions of varying consistencies within a tissue mimicking phantom. We suggest that this technique of applying high frequency vibration during sonography holds much promise for improved sonographic assessment of solid lesions of varying composition.
Health Sciences

School of Medicine and Health Sciences

Long-term Follow-Up After Immediate Postabortion IUD Insertion

Background

Long-term outcome data are lacking for intrauterine devices (IUD) inserted immediately after abortion. We conducted a study to determine long-term continuation and complication rates after immediate IUD insertion following elective surgical abortion.

Methods

We conducted a retrospective chart review of all patients who had IUDs inserted at the time of elective abortion in our clinic between February 2004 and September 2010. We reviewed all available records throughout our medical system for all service dates following IUD insertion. Three attempts were made to contact patients by telephone to obtain additional outcome data.

Outcome

We inserted 377 IUDs at the time of abortion, of which 216 (57.3%) were inserted following second trimester procedures up to 20 weeks gestation. Follow-up information was obtained for 282 women (74.8%). Only 33.9% attended their initial scheduled follow-up appointment. Follow-up data were available for 216 women at six months (57.3%) and 205 (54.4%) at one year after insertion. For women with follow-up data, continuation rates of the original IUD were 88.0% (190/216) at six months and 73.7% (151/205) at one year. Of those with follow-up, complication rates were not increased after second trimester abortion. IUD expulsion rates following first and second trimester abortion were 7.7% vs. 9.9%, respectively (p=0.4).

Conclusion

Intrauterine devices (IUD) may be safely inserted after first and second trimester abortion. Given poor return for follow-up after elective abortion, immediate postabortion IUD insertion can increase device utilization. At one year following IUD insertion, continuation rates following immediate placement after elective abortion are similar to that for the general population. Further study is needed to assess the cost-effectiveness, long-term continuation and reasons for IUD early discontinuation following immediate IUD insertion after elective abortion.
Yoga is a mind-body practice that incorporates a variety of techniques such as breathing, postural movement and meditation. These practices have shown to enhance and maintain physical, emotional, mental, and spiritual wellbeing. Patients on hemodialysis may benefit from yoga techniques by its positive influence on their exercise capacity, muscle strength and quality of life. We tested the hypotheses that patients on hemodialysis would be willing to participate in the intra-dialysis yoga study, no serious adverse effects would be observed from yoga practice and yoga would demonstrate a trend towards improved quality of life. Six hemodialysis patients were screened, enrolled and randomly assigned to participate in either a 12-week yoga intervention group with usual dialysis care or a non-intervention group with continued care. Feasibility was measured by collecting data on the participants’ willingness, frequency and capacity to practice yoga. All participants completed the Kidney Quality of Life (KDQOL) questionnaire at baseline and 12 weeks to measure quality of life. Data on adverse events related to yoga practice were also recorded. Among patients approached in the dialysis center, 74% reported interest in participating in the yoga study. There were no dropouts and follow-up was 100% in the active yoga intervention group. No serious adverse events were observed in the active group over the 12-week period. The KDQOL scores showed varying trends between the two groups. Data suggests that patients on dialysis are interested and willing to participate in yoga practice. Additionally, intra-dialysis yoga practice showed a good safety profile with the potential to enhance the quality of life of patients on hemodialysis.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Assessing Adolescent Views on Spirituality and Health

BACKGROUND

Previous research on adolescent attitudes towards religion and spirituality has shown that adolescents who are more spiritual or religious engage in less risky behaviors and use their spirituality to cope with physical illnesses more than their less spiritual or religious counterparts. An adult study by McCord et al. reported that the majority of adults in a primary care setting preferred to have their spirituality addressed by their physician in situations such as serious illness or loss of a loved one. A similar study was recently conducted by GWISH and the GW Department of Emergency Medicine with adults in the Emergency Department. Unlike adults, there is limited insight into adolescent understanding of religion and spirituality. The purpose of this study is to first determine adolescents’ level of understanding of spirituality and second, to assess their attitudes regarding attention to their spiritual needs by healthcare providers.

METHODS

We began designing the adolescent survey based on the existing quantitative adult survey, but found that the length and advanced level of language was not appropriate for adolescents. After administering the survey to a few adolescents, I discovered that the topic of spirituality can be quite abstract for adolescents, making the survey difficult for them to complete. Dr. Puchalski and I consulted Dr. Pat Fosarelli, a pediatrician, Doctor of Ministry, and survey expert, as well as our Children’s National Medical Center contact, Dr. Sabah Iqbal, to refine the study plan and develop a qualitative survey in order to arrive at more meaningful results.

RESULTS

A pilot survey was developed to be administered to 40 adolescent patients, ages 13-18, in the Emergency Department at CNMC. The survey consists of qualitative questions that will assess adolescents’ understanding of spirituality and how it impacts their health. The results of the pilot survey will inform the development of a larger survey to determine if and when adolescents prefer to have their spirituality addressed by their physicians.

CONCLUSIONS

While working on this study, I have gained invaluable experience with survey development. I am now capable of critically evaluating questions from the perspective of a researcher and potential participant. I have discovered that spirituality can be an abstract topic for adolescents, and it is therefore essential that the survey is concise and simple in order to accurately assess adolescent views on spirituality and health.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Reflections of a Medical Student Volunteer at Clinica Esperenza, Roatan, Honduras, Summer 2012

OBJECTIVES/BACKGROUND
As part of a community health track rotation experience, Mr. Rosenblatt volunteered at a community primary care clinic in Roatan, Honduras. Roatan, a Caribbean off the coast of Honduras, island only has one public hospital available for residents which is poorly funded and provides substandard care. Clinica Esperanza, a full primary healthcare clinic, was founded by Peggy Strangers, an American nurse to provide quality, affordable primary care to the residents of Roatan. Medical students rotating through the clinic perform duties of patient triage, working in the pharmacy and performing physical examinations and history taking. In addition to the above responsibilities, Mr. Rosenblatt performed vision screenings for school children in the community, and tested vulnerable populations for HIV.

METHODS
In order to arrange the community health activity, Mr. Rosenblatt contacted Clinica Esperanza and was approved to perform a basic medical school student volunteering session of two months.

RESULTS TO DATE
Mr. Rosenblatt was able to effectively volunteer for two months at Clinica Esperanza, fulfilling his requirement for the summer Community Health Track project at the School of Medicine. Mr. Rosenblatt was able to learn about practicing medicine and primary care resource poor settings, and gained valuable clinical experience.

CONCLUSIONS
The Community Health track summer project was a valuable experience, and Mr. Rosenblatt was able to apply the skills that he had learned in the first year of medical school in the clinical setting.
Layered Generative Learning: The Lived Experience of Advanced Sonographers

BACKGROUND
The purpose of this research was to gain insight into the essence of the journeys of six purposively selected nonphysician clinicians in sonography as they transitioned in their profession, from working as sonographers to becoming advanced sonographers.

METHODS
A single researcher conducted in-depth interviews (Seidman, 2006) and analyzed interview transcripts in keeping with transcendental phenomenology data collection and data analysis methodology (Moustakas, 1994).

RESULTS
This study found that these nonphysician clinicians sensed a need to push the bounds of their working knowledge of clinical reasoning and embarked on a trajectory of generative learning (Wittrock, 1992). Through such learning, they gained niche expertise (Ismail, 2012) in their profession and transitioned to a role of advanced practice, with increased responsibility and accountability for their work. The essence of their role transition, as shown in a proposed learning model, was that they engaged in layered generative learning.

CONCLUSIONS
Researchers and educators in occupations in which nonphysician clinicians contribute integrally to the physicians' expert work may explore the findings of this study. Researchers may investigate whether these learning journeys provide insight to other professions. Educators may design and test continuing education modules that provide just-in-time-learning for clinicians to prepare for professional advancement yet remain immersed in the context of their daily work. Scholars and researchers may investigate an implication of this study’s finding that in sonography diagnosis is a real time act inseparable from scanning. Researchers may study various facets of the concept of shared responsibility/accountability for the diagnosis, in diagnostic medical sonography.
A Brief Emergency Department Intervention to Reduce Cellphone Use While Driving

BACKGROUND

Distraction by cellphone use contributes to injury and fatal crashes. It is unclear if drivers understand the risk of using their phones.

OBJECTIVE

To assess the effectiveness of a brief written intervention in the ED aimed at changing drivers’ willingness to perform risky behaviors.

METHODS

Pre-Post intervention survey of non-critically ill, English speaking, ED patients at a single urban institution who regularly drove and used a cellphone. Subjects were asked on how many days in the past 30 and later how many days in the next 30 they intended to engage in the same behaviors. The intervention was a 5 point list describing the estimated increases in crash risk for each behavior. SPSS v19.0 performed Wilcoxon matched pairs ranked sign test for significance.

RESULTS

365 of 501 eligible patients consented (72.9%). Subjects’ median age was 36, 52.9% were female, and 51.5% were Black (37.3% White, 5.5% Hispanic). 66.8% routinely used their cellphone for email, 58.8% routinely used it to websurf, and 46.6% routinely used a hands-free device. Only 20.9% sent or received fewer than 30 texts/month. To make calls, 80.8% of subjects used a cellphone more often than a landline and 31.2% used ONLY a cellphone. Subjects were inaccurate at estimating crash risks. For low BAC (0.08 to 0.120), 22.2% knew the crash risk increases by about a factor of 3; 55.1% over estimated that risk. 19.3% correctly answered that using a cell to make a call without a hands-free/Bluetooth device increases risk by a factor of 3; 42.3% underestimated the risk. For making calls with a hands free device, 42.5% knew this increased the risk by 1.5 times but 20.5% believed using a hands-free device meant no increase in risk. Individuals could intend to change their behavior in either direction. Overall, the intervention decreased subjects’ intentions to engage in risky behavior (Table 1). However, for each behavior, a small percentage increased in their willingness to perform it; this effect was overcome by a larger number who were less willing to perform it.

CONCLUSION

After our brief written intervention in the ED, fewer subjects intended to engage in risky driving behaviors including riding with a drinking driver, driving after drinking, and using a cellphone to make calls, email, or text while driving.
Occupation or Profession? Plotting the Boundaries of Radiation Therapy

BACKGROUND
The purpose was to analyze the current boundaries of the radiation therapy profession, as perceived by directors of the Joint Review Committee on Education in Radiologic Technology (JRCERT) accredited radiation therapy educational programs, and to propose recommendations that might guide future research and practice capable of expanding these boundaries. Expanding our understanding of how individuals involved in the practice and teaching of radiation therapy perceive the state of their profession along the mentioned eight dimensions will help the development of approaches, methods, and content to strengthen and enhance the professional identity of radiation therapy. This understanding is essential, if radiation therapy is to plot a meaningful course of evolution along the path of professionalism. Only through such evolution can those involved in the education and practice of radiation therapy successfully integrate the unique technical and affective components that constitute a holistic professional identity.

METHODS
Eighty-one study participants were recruited from a convenience sample of radiation therapy program directors listed on the JRCERT website. The web survey was grounded in Pavalko’s occupation-profession model that measures professional evolution along the dimensions of: (1) theory and intellectual technique; (2) relevance to social values; (3) training period; (4) motivation; (5) autonomy; (6) commitment; (7) sense of community; and (8) code of ethics. Each dimension was assessed employing a four-point Likert scale.

RESULTS
Radiation therapy is closer to being a profession than an occupation. Participants indicate radiation therapy: has a sound theory and intellectual technique; inherently contains relevant social values in its practice; is guided by a well-developed code of ethics; has a fairly high sense of community; and offers a good deal of autonomy for its members.

CONCLUSIONS
The strong sense of community will likely continue to be the main driver of professional development in the 21st century. At a time when technology is becoming more prevalent and pervasive in the delivery of health care, radiation therapists are continuing their journey on the way from an occupation to a profession by very much cherishing their human touch.
Layered Generative Learning: The Lived Experience of Advanced Sonographers

BACKGROUND

The purpose of this research was to gain insight into the essence of the journeys of six purposively selected nonphysician clinicians in sonography as they transitioned in their profession, from working as sonographers to becoming advanced sonographers.

METHODS

A single researcher conducted in-depth interviews (Seidman, 2006) and analyzed interview transcripts in keeping with transcendental phenomenology data collection and data analysis methodology (Moustakas, 1994).

RESULTS

This study found that these nonphysician clinicians sensed a need to push the bounds of their working knowledge of clinical reasoning and embarked on a trajectory of generative learning (Wittrock, 1992). Through such learning, they gained niche expertise (Ismail, 2012) in their profession and transitioned to a role of advanced practice, with increased responsibility and accountability for their work. The essence of their role transition, as shown in a proposed learning model, was that they engaged in layered generative learning.

CONCLUSIONS

Researchers and educators in occupations in which nonphysician clinicians contribute integrally to the physicians’ expert work may explore the findings of this study. Researchers may investigate whether these learning journeys provide insight to other professions. Educators may design and test continuing education modules that provide just-in-time-learning for clinicians to prepare for professional advancement yet remain immersed in the context of their daily work. Scholars and researchers may investigate an implication of this study’s finding that in sonography diagnosis is a real time act inseparable from scanning. Researchers may study various facets of the concept of shared responsibility/accountability for the diagnosis, in diagnostic medical sonography.
Freidreich Ataxia (FA) is a progressive degenerative disorder. Symptoms typically appear in children between 5 and 25 years and the mean age of death is approximately 15 years after the onset of symptoms. A more recent understanding of the pathogenesis of the disease and new trial therapies has increased the need to understand the typical progression of mobility limitations. The purposes of this study was to determine the progressive use of assistive devices in a population of children with Freidreich Ataxia as well as the potential impact of children's attitudes towards the use of the device.

Methods
This is a descriptive study using a mixed qualitative and quantitative design. Following IRB approval, a semi-structured telephone interview protocol including both open and closed ended questions gathered information about the children's progressive use of mobility devices as well as their attitude towards their effectiveness. Responses to closed-ended questions were summarized using descriptive statistics. Responses to open-ended questions were analyzed using qualitative methods.

Results
30 children whose parents agreed to participate in the interview included: 18 males and 12 females, ranging in age from 9 to 17 years, with a mean age of 13.8 years. Subjects reported using a variety of assistive devices that changed as the disease progressed. Of the 30 children, 19 reported they used foot orthoses, 7 used body jackets, 3 used canes, 1 used crutches, 14 used walkers, and 19 used wheelchairs. The mean age subjects began using a wheelchair was 13.0 years. The greatest determining factor in the type of assistive device used was their current impairments and functional limitations. Other factors that emerged influencing the selection of assistive device included: energy conservation, cosmesis, community mobility, accessibility in the home, and safety. Of the 19 wheelchair users, 8 began using a wheelchair without first using a walker. Subjects and families preferred a wheelchair secondary to their perception of increased safety, cosmesis, community access, and improved energy conservation provided by the wheelchair in contrast to the walker.

Conclusions
A wide variety of assistive devices are used by the Freidreich Ataxia population. Most often, the choice of which device to use is made based on the current functional status of the subject. Other important factors impacting this decision include cosmesis, safety, accessibility, and energy conservation. Information about the progressive use of assistive devices in this population may assist in evaluating the impact of new therapies on the disease progression.
SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Trends in the Rates of Computed Tomography Use and Diagnoses of Pulmonary Embolism and Pneumonia in Emergency Departments

BACKGROUND

In the past decade, Computed Tomography (CT) use in U.S. emergency departments (ED) has increased dramatically. Objective: We described recent trends in CT use for potential symptoms of pulmonary embolism (PE). We also assessed if patient, hospital, or regional characteristics accounted for a disproportionate share of testing growth.

METHODS

We used the 2001-2009 National Hospital Ambulatory Medical Care Survey, a nationally representative survey of U.S. ED encounters. Patients were included with at least one of three common reasons for visit with PE symptoms (chest pain, dyspnea, or hemoptysis). Linear regression analysis was used to calculate increases in CT use over time. Relative and absolute increases in use were compared qualitatively among subgroups (age, gender, race, insurance status, immediacy of visit, geographic region, and hospital characteristics).

RESULTS

The percentage of ED visits involving three common PE symptoms where a CT was performed increased from 2.6% in 2001 to 12.5% in 2009, a five-fold increase, with an average growth rate of 20.9% (95% confidence interval [CI] 14.1–28.2) per year. There was an increase in testing rates in every subgroup. The lowest growth rate was among Hispanics, whose CT rates grew 10.2% (CI 4.7-12.0) per year and increased from 4.3% in 2001 to 8.2% in 2009. The highest growth rate was in non-urban hospitals, whose CT rates grew at 31.3% (CI 14.3-50.8) per year and increased from 0.6% in 2001 to 7.9% in 2009.

CONCLUSION

There was a dramatic increase in CT use from 2001 to 2009 in patients with PE symptoms. All subgroups appear to have experienced increases, some more than others. Specifically, subgroups with low rates at baseline have experienced the highest rate of increase. Future studies should examine how this practice change has impacted outcomes for both patients tested and for those ultimately diagnosed with PE.
School nurses and primary care providers: Collaborating to improve asthma self management in school aged children

OBJECTIVES:
1. To assess current school nurse practice and system level factors in Massachusetts affecting asthma management in school aged children.
2. To assess the degree to which School Nurses (SNs) collaborate with Primary Care Providers (PCPs)/team members in the community to improve asthma management practices in school children.
3. To identify barriers and facilitators to managing asthma in schools

METHODS

Design: Web-based survey

Using findings from two focus groups, a survey tool was constructed, pilot tested for comprehension and clarity by a group of approximately 15-20 SNs and revised accordingly. In April 2010 the survey was sent to a sample of approximately 2100 SNs in Massachusetts using a link to an encrypted SurveyMonkey site. IRB approval was gained by the Boston College Institutional Review Board.

Data Analysis: Survey analysis used descriptive/qualitative methods to elaborate on the current asthma management practices in the schools and barriers and facilitators to collaboration between SNs and primary care practices.

RESULTS/FINDINGS

598 SNs responded to this survey with a response rate of 28.5% and of these 433 usable responses were analyzed. Only 3% of the respondents reported they did not communicate with PARENTS about asthma symptoms. 77% of the SNs felt that this communication with parents was good to excellent. Parental notification (94%) and medical history/exam form signed by provider (92%) were the two most common methods. 70% of SNs reported that learned that some students had asthma when they visited the health office for asthma symptoms. More than half of SNs identified a lack of communication with health care providers as a barrier to effective asthma management. Only 32.3% felt that the communication with primary care providers (PCPs) was good/excellent and even fewer (22.4%) reported this level of communication with allergy specialists. The telephone was also the most popular method of communicating with primary care providers (47.1%), followed by fax (18.5%), written notes (14.8%) and e-mail (2.8%). Only 56.7% of those with Asthma Action Plans (AAPs) had sufficient information on the AAP and lack this tool was identified by SNs as being the most frequent obstacle to managing asthma in the schools. Further quantitative analyses will be presented on relationships between demographic variables and asthma management practices.

CONCLUSIONS

Models are needed that improve collaboration around asthma management for school aged children between PCPs (PNPs and pediatricians) and SNs in order to truly reflect an interdisciplinary, community based, and system level intervention.
Summer in Spain—Research & Clinical Experiences

This summer GW offered the first ever internship program for 1st year medical students at Universidad de San Pablo in Madrid, Spain. This program was 8 weeks long and involved work at three different sites in Madrid: the IMMA laboratory (Institute of Applied Molecular Medicine), Hospital de Monteprincipe and Hospital de San Chinarro. Students participated as research scientists for four weeks at the IMMA laboratory. The following four weeks continued with ongoing research at the IMMA but also integrated two to three days of work each week at the Hospital de Monteprincipe or Hospital de San Chinarro in the Emergency Department as well as the Department of Surgery. This allowed for students to be a part of the healthcare system in Spain on both the medical research and primary care level.

At the IMMA, the research project involved evaluation of the distribution of the S100 protein in neurological tissue such as spinal tissue and brain tissue. This protein has particular relevance to various neurological diseases such as tumors and ischemic disorders. Since this project was in the early stages of research, the role of GW students was to complete various immunohistochemical experiments to determine which types of staining procedures were optimal for viewing this protein distribution in various types of tissues. Most of the tissues were from rat and mouse models of various diseases but towards the later stages of this project students were able to stain human tissue samples that were received as donations to scientific research from the Hospital de Monteprincipe. Eventually high-quality pictures of the S100 protein distribution in various neurological tissues were able to be captured. This will be further analyzed for patterns in its distribution among the tissues. Eventually, this research will be published in a medical Spanish journal upon completion.
HEALTH SERVICES

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Health Promotion at the Community Level in Cabracancha, Peru

Funding from the George Washington University School of Medicine and Health Sciences Health Services Scholarship was used for travel to Peru for eight weeks from late June to August of 2011. During this time, public health projects promoting measures to prevent water-borne and fecal-oral infections were implemented in the elementary and high schools, the local health post, and the regional hospital, Hospital Regional Jose Soto Cadenillas. In addition, the Health Services Scholarship funds allowed for rotations on the obstetric, medicine, surgical, and emergency services at the hospital.

Cabracancha is a rural community located in the Andes Mountains of north-central Peru, just seven hours south of the Ecuadorian border. Daily living is associated with tending farm animals and cultivating potato and corn fields. The area enjoys rain almost nine months of the year and has a consistent climate that is warm during the day and can become very chilly at night. Illiteracy is high, and many young girls cease their education after completing elementary school. As would be expected for a community with limited resources and education, the rates of preventable disease are disturbing.

Projects included encouraging young students to identify the public health risks in Cabracancha. In these projects the participants discussed and learned about means to sanitize their water supply, encourage hand hygiene in their homes and at school, and to properly use latrines for personal needs. In the health post, mothers from the community learned the importance of maintaining clean cooking spaces and enforcing strict hand washing rules in their homes. Improper hand hygiene is consistently identified as the culprit for the majority of parasitic infection in this part of Peru.

In one highlighted project, elementary school students collaborated to produce essays and posters, which were presented to clinicians from the regional capital of Chota. Their work was evaluated by the clinicians and the top performing projects received a monetary award and a medal, encouraging further work and awareness about the health of their community.

During hospital rotations, there was opportunity to assist in general surgery and cesarean sections, change surgical wounds for hospitalized patients, assist in over twenty-five births, collaborate with physicians on night call in the emergency service, examine and evaluate patients on the medical service and in outpatient clinic, and speak with patients and their families about diagnosis, expected clinical outcomes, and the importance of following medication regimens upon discharge from the hospital.
Classification of Emergency Department CT Imaging Reports using Natural Language Processing and Machine Learning

BACKGROUND

The recent emphasis on health information technology has highlighted the importance of leveraging the large amount of electronic clinical data to help guide medical decision-making. In this research, we use natural language processing (NLP) and machine learning techniques to classify patient reports based on their outcomes. NLP generates a structured output from computed tomography (CT) reports, which are then coded for the presence of orbital fractures for blunt facial trauma victims.

Retrospective chart review of consecutive computed tomography (CT) imaging reports for patients suffering blunt facial trauma was conducted over 26 months at two urban hospitals. Staff radiologists dictated each CT report and the outcome of acute orbital fracture was extracted by a trained data abstractor, with a random subset checked by a study physician to confirm its reliability. Among the 3710 reports, 460 were positive for orbital fracture and 3250 had a negative outcome.

METHODS

Our system takes patient reports as input to the Medical Language Extraction and Encoding (MedLEE) (a biomedical NLP tool) to tag patient reports with Unified Medical Language System (UMLS) codes and modifiers that show the probability and temporal status. After this tagging process, the output is filtered to exclude findings with low certainties or findings linked with patient’s history or future modifiers. These filtered findings are then combined with their associated outcomes, and a single file is generated in attribute relation file format (arff) as input to data mining tool WEKA 3.6.4 for classification. In WEKA, this file is converted to a word vector representation and decision tree classification with 10-fold stratified cross-validation is applied.

RESULTS

Our results obtained using NLP shows improvement over classification using raw text. Precision goes up from 0.943 to 0.966, recall goes up from 0.944 to 0.965 and f-score increases from 0.943 to 0.966.

CONCLUSIONS

Biomedical NLP and machine learning techniques appear to be promising in developing a support system for clinical decision making. As future work, different classification algorithms and different feature selection criteria will be researched for more efficient and accurate results.
Discrimination, acculturation, and desire for control over healthcare among breast patients receiving patient navigation

Identification of patients’ feelings of discrimination, acculturation, and desire for control over their own healthcare could assist patient navigators and providers in delivery of recommended care. We examined scores on three validated instruments: the Discrimination Scale (race and SES), Marin Acculturation Scale (MAS), and the Wallston Desire for Control over Healthcare (DCON), among 989 navigated patients with suspicious breast findings or cancer who presented at sites participating in a navigation effectiveness study. We used analysis of variance to understand the impact of marital status, household size, number of dependents, employment status, insurance status, income, education, and use of a primary care physician on the respective scale scores while controlling for race, age, and ethnicity. Neither the Discrimination Scale race subscale nor the SES subscale were related to any of these factors. The full models for the MAS were also non-significant but there was a tendency for more acculturated patients to have no insurance and to be employed full-time compared to their less acculturated counterparts. All models examining the DCON scores were highly significant but these findings were driven by the highly significant findings for race and ethnicity in the models (p range: 0.0273 to <0.0001) – non-Hispanics tended to want more control over their healthcare than Hispanics and patients of other races desired more control than either whites or blacks. Examining age, race, and ethnicity each in comparison to each of the scale scores revealed that the DCON was significantly related to race, age, and ethnicity (all p <0.0001) with other races wanting the most control compared to whites and blacks, younger subjects wanting more control than older subjects and non-Hispanics wanting more control than Hispanics. The Discrimination scale SES measure was significantly related to age (p=0.0357), race (p=0.0332), and ethnicity (p=0.0017). There was a tendency for SES discrimination to decrease with age and for whites to experience less SES discrimination than blacks or other races. The Discrimination scale race measure was significantly related to age (p=0.0441) with a tendency for discrimination to decrease with age. We conclude that patients’ demographic background is associated with feelings of discrimination, acculturation, and desire for control over healthcare. These data could be useful in targeting interventions or identifying individuals who may have attitudinal barriers to needed cancer care.
HEALTH SERVICES

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Physician Assistants in the United Kingdom: An initial profile of the profession

OBJECTIVE

To characterize the Physician Assistant (PA) profession in the United Kingdom for the first time.

DESIGN

Online questionnaire made available to all UK physician assistants and physician assistant students.

SUBJECTS

All physician assistants and physician assistant students in the United Kingdom in 2011.

MAIN OUTCOME MEASURES

Specialty choice, location, scope of practice, and previous clinical experience of UK physician assistants and physician assistant students.

RESULTS

Of 165 physician assistants and physician assistant students in the United Kingdom on 31 December 2010, 127 (77%) responded to the survey. 81% of PA students (76/94) and 72% (51/71) of PAs responded. PAs are working in 19 different medical and surgical specialties. Recently graduated physician assistants are more likely to practice in secondary care than more experienced physician assistants. PAs are working throughout England, but are concentrated near PA training programs, with 61% (31/51) of PAs practicing in the West Midlands and London. Scope of practice varied according to the needs of the specialties in which the PAs practice. Prior to undertaking physician assistant training, respondents worked in a wide variety of health professions, most commonly as health care assistants (19), nurses (19) or paramedics (15).
Examining HIV/AIDS Knowledge, Attitudes and Practices in Buwagogo Sub-county, Uganda; A Qualitative Study

BACKGROUND
A community initiative facilitated by The AIDS Support Organization focusing on HIV/AIDS education, prevention and treatment, has existed for the last 14 years. The purpose of this study was to examine knowledge of HIV/AIDS transmission and prevention; attitudes toward HIV/AIDS status disclosure, antiretroviral therapy and people living with HIV/AIDS; and self-reported HIV/AIDS risk behavior among adult females and males (age 18+) and key leaders in Buwagogo sub-county.

METHODS
Previously collected qualitative data were analyzed from a qualitative exploratory study. Data were obtained from four focus group discussions with women, men, youth, and HIV+ clients and nine in-depth interviews with key opinion leaders. Thematic content analyses were performed manually.

RESULTS
Risk factors in acquiring HIV/AIDS, related to cultural/economic practices such as inheriting widows, property grabbing, burial ceremonies, circumcision celebrations and migrant workers. Women were perceived as the most susceptible population to acquire HIV and men and women both explained there was stigma in regards to condom use. Discrimination towards people using anti-retroviral therapy was described and people feared to disclose one’s HIV/AIDS status among both community and family members.

CONCLUSION
Buwagogo community has described The AIDS Support Organization as being a major player in helping reduce HIV/AIDS within the sub-county; however, it is apparent that stigma and cultural and gender norms play a substantial role in the prevention and treatment of HIV/AIDS. Recommendations include: programs targeting income, livelihood, literacy, health and legal needs of women, establishing a support system for the widowed, integration of faith-based networks, and programs reducing stigma related to condoms, people living with HIV/AIDS and antiretroviral therapy.
HIV/AIDS

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Report On Prevention programs for HIV Positive Men Who Have Sex with Men from Selected State Health Departments

BACKGROUND

The HIV epidemic in the United States varies greatly between states, and a multitude of interventions have been implemented to combat the rise in HIV cases. The group with the largest risk is Men who have Sex with Men (MSM), which represents more than half of all cases in the United States. Prevention among positives (PreP) is a relatively new technique being utilized in this group, reducing community transmission levels and preventing new cases.

METHODS

Data for this study were collected through key informant surveys of eight state level health departments on their PreP interventions among MSM. Results from the qualitative surveys were coded and scored, and three successful programs were chosen representing differing levels of epidemic and resource allocation. These programs were then analyzed and disseminated to all states through The National Alliance of State and Territorial AIDS Directors (NASTAD) to increase awareness of these interventions.

RESULTS

The three successful programs highlighted through this study include interventions include Partnerships for Health – a specific Diffusion of Effective Behavioral Intervention (DEBI), Treatment Linkage to Care, and Comprehensive Risk Counseling and Services.

CONCLUSION

The cultural understanding of the MSM community is critical to the success of these programs as well as the newly released CDC funding application for high risk communities.
Background

The influences of parenting styles and practices on adolescent sexual behaviors are well-documented in the United States. Little research has been done on the social contexts of adolescent sexual behaviors in sub-Saharan Africa. Instruments for measuring constructs such as parental monitoring may not be suitable for use in African settings for a variety of reasons.

Methods

As part of a longitudinal cohort study of N=1275 teenage girls and boys in two Ghanaian towns, we developed a 26 item interviewer-administered questionnaire module intended to assess four dimensions of youth-adult relationships: conflict, support, monitoring, and financial support. Each item is worded: “There is an adult in my life who....” Illustrative interactions include: “Gets mad at you,” “Listens to you,” “Knows where you are at night,” and “Provides for your necessities.” We assessed the reliability and validity of the four proposed scales through a series of analyses.

Results

Confirmatory factor analyses supported our four-factor model. Fit indices were within the acceptable ranges, as were factor loadings for all but four items. After removing those items, Cronbach’s alphas for the resulting conflict, support, monitoring, and financial support scales were 0.73, 0.80, 0.73, and 0.82. The pattern of bivariate associations between each of four scale scores and select sociodemographic variables were consistent with expectations, providing evidence of the known-groups validity of the scales. For example, girls were more heavily monitored than boys; older youth experienced more conflict with adults and less support, monitoring and financial support than younger youth; and youth living with neither biological parent received less support, monitoring, and financial support than youth living with both biological parents. In bivariate logistic regression models, conflict was positively associated with self-reported sex, and support, monitoring, and financial support were all negatively associated with it (Odds Ratios = 1.66, 0.74, 0.47, and 0.60). In a multivariate model including all four scales and controlling for several sociodemographic variables, the effects of conflict and monitoring on self-reported sex remained large and statistically significant (Adjusted Odds Ratios = 1.49 and 0.64).

Conclusion

The instrument is practical for use in sub-Saharan African settings and produces measures of four dimensions that are reliable, valid, and predictive of sexual behavior in youth.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Clinical Experience at Nyumbani Children’s Home

My summer Global Health Track project led me to Nairobi, Kenya, where I involved myself with numerous aspects of the Nyumbani program. Nyumbani, which means “home” in Kiswahili, serves as an orphanage for 110 children with HIV who have lost both parents. The program not only provides free anti-retroviral (ARV) treatment to the children living there, but also serves as a respite center for critically ill children around Nairobi. Living at the orphanage, I was able to interact with the kids on a daily basis, observing the standard of care they received as well as assisting in after-school tutoring. Most of my clinical experience came from volunteering at the Lea Toto clinic in Dagoretti, which provides free of charge community medical services to HIV positive children living within resource poor communities in Nairobi. My clinic mainly offered monthly maintenance care, including prescription refills and check ups. We assessed viral load, treated opportunistic infections, confirmed adherence to their ARV’s, and provided nutritional counseling. We also held health education workshops to teach patient’s and their families the importance of adherence to medications. Alongside social workers, we conducted unannounced home visits once a week where we assessed and addressed basic needs of the families, such as food, water, and proper sanitation practices. Overall, we learned the importance of the caregiver’s role and general awareness in effective treatment of children with HIV. Attending gender-based violence meetings, I also developed a better understanding of the spread of HIV, given that the polygamy rate of males in these communities is 80%. Overall, this invaluable experience allowed me to survey the interdisciplinary impact of this program on the disadvantaged community by observing the interplay between economic, social, and cultural forces at work in mitigating the effect of HIV/AIDS in the pediatric population.
HIV/AIDS

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Interactions between NF-κB monomers and IkB in Latently HIV-1 Infected Cells

BACKGROUND

Despite the use of highly-active anti-retroviral therapy (HAART) in HIV therapy, the ability of HIV-1 to establish latency within host cells remains a major obstacle in the successful treatment and cure of HIV infection. The NF-κB signaling pathway is believed to be central to the transcription and activation of latent HIV provirus. Stimulation of this pathway initiates the protein degradation of cytoplasmic inhibitory-κB molecules (mainly IkBa, IkBb, and IkBe). This releases bound NF-κB dimers and allows them to translocate to the nucleus to activate gene transcription, including that of HIV-1 provirus. NF-κB dimers can exist as a homodimer or heterodimer of any of five monomeric subunits (RelA, RelB, c-Rel, p52, or p50). Previous work by our lab has shown an important role of the IkBe isoform in stimulating HIV from latency, thus we examine its role and that of the other two isoforms here.

METHODS

In order to determine the protein kinetics of IkB isoforms during proviral activation, we stimulated HIV-1 latently infected (U1) cells with a TNF-α. Protein levels of IkBa, IkBb, and IkBe were measured using Western Blot analysis. To determine the protein—protein interactions between individual NF-κB monomers and IkB molecules, a series of immunoprecipitation reactions were performed with U1 whole cell lysates. We isolated IkB isoforms using either anti-IkBa, IkBb, or IkBe antibodies. Western Blots were then performed using various antibodies against the five monomeric forms of NF-κB.

RESULTS

Following TNF-α stimulation, IkBa protein was rapidly degraded to undetectable levels and raised and peaked at 60 minutes post-induction. IkBb and IkBe levels, demonstrated similar kinetics at a slower rate. Results of the immunoprecipitation experiments are pending, although several interactions have been demonstrated between IkBa, IkBb, and IkBe isoforms to NF-κB monomers p50, p52, or RelA. Of interest is the increased association of IkBe with the RelA monomer, relative to p50 or p52.

CONCLUSIONS

The increase in protein levels of IkBa following TNF-α stimulation are opposite to the IkBa mRNA kinetics observed by our lab, previously. This may be explained by the negative regulatory role of NF-κB dimers in stimulate the expression of IkB proteins. We suspect that the greater association of RelA to IkBe, relative to p52 or p50 observed, reflects an increased affinity of IkBe for the RelA subunit. As the RelA-p50 dimer has been shown to be a proviral activator, modulation of the IkBe system may serve as a novel approach to activating latent HIV.
**Losses to Follow-up Among Patients Registered for Care at a Tertiary HIV Referral Center in Chennai, India**

Highly active antiretroviral therapy (HAART) has dramatically improved survival and transformed HIV into a chronic disease requiring long term follow-up of HIV infected patients. India has approximately 2.3 million HIV-infected persons and Antiretroviral Therapy (ART) is available in India via the public and private sectors. While services such as physician consultation and ART costs in the government sector are free, patients are generally required to pay for these and other services in the private sector. There are limited data on loss-to-follow up (LTFU) rates and factors associated with LTFU in India.

Our case control analysis comprised a subset of patients registered for care at YRGCARE (a private non-governmental organization providing HIV clinical services in Chennai since 1993) between 01/01/2004 and 12/31/2009. Cases (LTFU) were defined as patients who did not have at least one visit between 01/01/2010 and 12/31/2010. “Project” patients included the subset of patients who were enrolled in clinical trials or projects and received some compensation for clinical care (e.g., free ART, free consultation, compensation for travel, etc.) and who were assigned retention staff. Logistic regression was used to identify factors associated with LTFU.

Of 7,995 patients included in the analysis, 68.2% were male with a median age of thirty-four. The overall loss to follow-up rate was 38.1 per 100 p-y. Among those who were LTFU, there were 304 (3.8%) documented deaths. In univariate analysis, LTFU was less common in those with higher baseline CD4 count, higher CD4 count at last visit to the clinic, being enrolled in a project and having initiated ART. LTFU was more common among patients who were older and unmarried. In multivariate analyses, persons were significantly less likely to be LTFU if they were enrolled in a project (OR: 0.66; 95% CI: 0.58, 0.77), being initiated on ART (OR: 0.32, 95% CI: 0.26, 0.38) or married (OR: 0.71, 95% CI: 0.57, 0.88).

This clinical cohort exhibited a high-rate of LTFU as the majority of the losses occurred within the first month. Given the negative association of LTFU with being enrolled in a project, innovative strategies using incentives (e.g., conditional cash transfer, travel incentives) and peer-health workers in improving retention among patients needs to be evaluated for efficacy and cost-effectiveness. Given the high rate of mortality among patients LTFU compared to documented deaths in the clinical cohort, the impact of these deaths on survival analyses need to be examined.
Systematic review and meta-analysis of tuberculin skin test responses in HIV-infected patients in resource-limited settings: implications for implementation of isoniazid preventive therapy

BACKGROUND

HIV-infected patients who have a positive tuberculin skin test (TST) benefit from isoniazid preventive therapy (IPT) but those with negative tuberculin skin tests do not. To accelerate scale-up of IPT, revised World Health Organization guidelines now explicitly state that assessment of TST is not a requirement for initiation of IPT as this test is difficult to implement in programs in developing countries. Untargeted use of IPT, however, may be inefficient use of resources and may result in adverse effects in some patients who are unlikely to benefit. We conducted this study to determine what proportion of HIV-infected patients in developing countries test TST-positive and may therefore derive benefit from IPT.

METHODS

A systematic review was conducted in order to determine the proportions of HIV patients testing TST-positive (induration ≥5 mm) and TST-negative in low- and middle-income countries. We searched Embase, Global Health, Medline and Web of Science for potentially relevant citations. A meta-analysis using a random-effects model was conducted on studies selected on the basis of country TB prevalence >100 per 100,000 population, availability of appropriately CD4-stratified data, study size and quality, and patient recruitment from HIV care services.

RESULTS

The search yielded 2,871 potentially relevant citations of which 226 were selected for full-text review. Data from 16 eligible studies included 8,007 patients from sub-Saharan Africa, Asia and Central and South America were summarized. The median proportion of patients testing TST-positive among these studies was 25.2% (IQR, 20.7-38.5) overall. For the 13 studies (7,482 patients) with appropriate data stratification, the median proportions of patients testing TST-positive with CD4 cell counts of <200, 200-499 and >500 cells/µL were of 14.3% (IQR, 11.1-19.3), 28.4% (IQR, 20.1-35.7) and 37.4% (IQR, 31.3-53.5), respectively. Five studies (5,567 patients) from Senegal, Uganda, Botswana, Mexico and Thailand were included in a meta-analysis to derive pooled summary estimates that were very similar to data from the larger group of studies. Overall, 23.5% (95%CI, 19.6-27.4%) of all patients were TST-positive. The proportions with CD4 cell counts of <200, 200-499 or >500 cells/µL who were TST-positive were 12.8% (95%CI, 10.5-15.1), 27.9% (95%CI, 23.0-32.8) and 41.6% (95%CI, 33.0-50.3), respectively.

CONCLUSIONS

We found that a minority of HIV-infected patients were TST-positive, even in high TB prevalence settings, and that the proportion testing positive was strongly associated with CD4 cell counts. These data should be carefully taken into account when deciding whether assessment of TST status should be included when implementing IPT programs.
INSTITUTE FOR BIOMEDICAL SCIENCES

Virus-Producing Cells Determine Host Protein Profiles of the Cores of HIV-1 Virions

BACKGROUND

Upon HIV entry into the target cell, viral cores are released and rearranged into reverse transcription complexes (RTCs), which support reverse transcription and also protect and transport viral cDNA to the site of integration. RTCs are composed of both viral and cellular proteins originating from producer cells, but only a fraction of the cellular RTC proteins has been characterized.

METHODS

We examined the proteomic profiles of the host cellular proteins in the cores of HIV-1 virions assembled in different types of HIV-1 host cells – Sup-T1 (T lymphocytes) and PMA-activated THP1 (model of macrophages, mMF). We performed LC-MS/MS analysis of the viral cores purified from HIV-1 NL4-3 virions by centrifugation through detergent-overlaid equilibrium density gradient. Potential involvement of identified proteins in the early stages of HIV-1 infection was assessed using gene ontology information and data from genome-wide screens on proteins important for HIV-1 replication. Infectivity of the viruses was assessed in TZMbl cells. Accumulation of cDNA and integration were quantified by real-time PCR.

RESULTS

We identified 181 cellular proteins incorporated in the cores of HIV-1 virions (T cells: 121, mMF: 107); 48 proteins were detected in all analyzed viral cores. The RNA binding (28), DNA binding (11), cytoskeleton (13), cytoskeleton regulation (15), chaperone (16) and vesicular transport (10) proteins were the most abundant. Cores from the virions assembled in SupT1 cells contained twice as many RNA binding proteins as cores from THP1-derived virus, while cores of virions assembled in mMF were enriched in components of cytoskeleton and vesicular transport machinery. At least 7 proteins earlier identified as important for virion organization or post-entry infection events were detected in the viral cores from both cell types (RHA [confirmed by Western blot], RCC2, UPF1, clathrin, Rab6, AIP1/ALIX, and Hsp70); 3 proteins – only in T cell-derived cores (DDX3, HNRNP, AIP/ERK2 IP 1), and 4 proteins – in mMF-derived cores (DDX21, dynein, ACTR3 and Impβ2). Viruses assembled in T cells and mMF demonstrated similar reverse transcription efficiency and infectivity.

CONCLUSIONS

Our data show that profiles of host proteins packaged in the cores of HIV-1 virions depend on the type of producing cells. While almost 60% of cellular proteins in viral cores assembled in T cells and mMF are different, the efficiency of the early infection caused by these viruses is similar, suggesting that most important host proteins are the same in the virions from different cell types and incorporated specifically.
The Contribution of Pulmonary Hypertension to Mortality in HIV-Infected Veterans in Washington DC: A 20-year Perspective

BACKGROUND
HIV has developed into a chronic, manageable infection in those offered antiretroviral therapy (ART). HIV is an independent risk factor for the development of pulmonary hypertension (PH) and contributes to morbidity and mortality.

METHODS
We identified veterans enrolled in the DCVAMC Primary-Care HIV Clinic with a diagnosis of PH (HIV/PH+) between 1989 - 2009. Retrospective review of our comprehensive electronic medical record (Vista_CPRS) was supplemented with paper-charts. Age-gender-year of HIV-diagnosis matched (3:1) controls (HIV/PH-) were identified. Demographics, co-morbidities and clinical and laboratory data relevant to both diseases were collected. Initial and follow-up EKGs, 2DEchos were reviewed.

RESULTS
89 subjects were identified: 22 HIV/PH+ and 67 matched HIV/PH- controls during the 20y study period. Subjects were predominately African-American (85%) and all were male. At PH diagnosis, mean age was 49.8y ± 11.0y; they lived 3y with PH on average. The all-cause mortality among HIV/PH+ was significantly higher (17/22, 77.3%) when compared to HIV/PH- (28/67, 41.7%, P= 0.006). At diagnosis, CD4 was 367.4 ± 250.2 cell/mm3; only 25% were on ART and 13% had achieved viral suppression. Nadir CD4 counts were not significantly different between groups. Among PH+, the frequency of drug abuse was (61%), HTN (44%), COPD (28%) and VTE (28%) with only the incidence of CHF significantly greater in the PH+ compared to PH- patients (56 vs 2%, p=<0.001). Where data was available, 43% (6/14) of PH diagnoses were incidental. In making a diagnosis, 6/14 (43%) had right atrial enlargement on EKG and for those with 2DEcho, initial pulmonary artery systolic pressure was 56 ±18 mmHg with a mean ejection fraction of 51% ± 15%, with no significant change on serial studies. Right heart catheterization and approved pharmacologic interventions were infrequently employed, smoking cessation was the main treatment modality.

CONCLUSION
All-cause mortality was high for our cohort and significantly greater for HIV-infected patients with PH when compared to those without PH. Contributing factors include medical co-morbidities, age and a presentation with PH when ART had not been initiated or viral suppression achieved. We found CHF was an important factor associated with the development of PH in our patients, also possibly contributing to overall mortality. Preemptive screening for dyspnea, with early referral for echocardiography, appear warranted in HIV+ patients. HIV providers need to pay particular attention to those with or at risk for the development of CHF and employ risk-reduction strategies, including initiation of ART and managing co-morbid conditions.
Comorbid Mental Illness, Social Support and HAART Medication Adherence in Youth Living With HIV/AIDS

BACKGROUND
The development and widespread usage of highly active antiretroviral therapy (HAART) have redefined treatment strategies for those suffering from HIV/AIDS. Medical care is now administered more like a chronic illness than a terminal disease, thus, making disease management extremely important for those living with HIV/AIDS. While adherence to HAART is one of the major treatment goals for these patients, several factors contribute to sub-optimal adherence levels and subsequent drug failure. With 50% of those living with HIV/AIDS meeting the criteria for one or more psychiatric disorders, the high prevalence of comorbid mental illness presents a significant challenge to effective disease management. Given the alarmingly high rates of HIV/AIDS in Washington, DC, especially among youth, a critical need exists to better understand the effects of mental illness on quality of life, disease management and medication adherence in this population.

OBJECTIVE
This study aims to assess the effects of mental illness on disease management in youth living with HIV (YLH) and adherence to highly active antiretroviral therapy (HAART). Additionally, social support will be examined as a moderator in the relationship between the prevalence of mental illness and medication adherence.

METHODS
A sample of 150 YLH between ages 13 to 22 were recruited from two clinics at the Children’s National Medical Center. A 90-minute computer-assisted (ACASI) survey was administered at baseline, 3-, 6-, 9-, and 12-months assessing various behaviors, coping styles, levels of social support and self-reported mental illness. In addition to the ACASI survey, medical records were reviewed in order to collect data regarding any clinical diagnoses of mental illness among participants. Viral loads were also collected and analyzed to determine HAART medication adherence.

RESULTS
A linear regression will be used to identify a relationship between mental illness diagnosis and medication adherence, as well as determine whether various levels of social support have a significant moderating effect on this relationship.

CONCLUSION
The results of this study provide insight into the contributing factors affecting disease management in YLH. Implications for the development of interventions and future research regarding secondary prevention and disease management of HIV are provided.
SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Patterns of Sexual Behavior Among Adolescents Perinatally-Infected with HIV

BACKGROUND AND OBJECTIVES
Perinatally HIV-infected children are entering adolescence and engaging in sexual relationships. The objective of this study is to describe patterns of sexual behavior among perinatally HIV-infected adolescents enrolled in an urban pediatric HIV specialty clinic.

METHODS
A retrospective chart review of perinatally HIV-infected adolescents aged 13 to 20 years enrolled in a pediatric HIV specialty clinic during a one-year period was conducted.

RESULTS TO DATE
Seventy seven charts were reviewed (57.3% male, 42.7% female, median age=16). One third (29.3%; n=22) had disclosed being currently sexually active or sexually active at some point in the past. Significantly more males (59.1%; n=13) than females (40.9%; n=9). The mean age of sexual debut was 15.92 and 15.89 years for males and females, respectively. The majority (63.6%; n=14) of patients disclosed having vaginal sex, with 9.1%(n=2) reporting oral sex, and 4.6%(n=1) combined vaginal and oral sex, and 22.7% (n=5) not disclosing the nature of sexual contact. All were heterosexual and were disclosed to about their HIV status. The mean number of lifetime partners was 1.4(SD=1.1) with a range from 1 to 5. Mora than half (54.6%; n=12) reported condom use 100% of the time, while 9.1%(n=2) reported not using condoms. Sexually transmitted infections (STI) were documented in 9.1% (n=2) and all were Chlamydia cases. One male reported a pregnancy in his partner. One female had 3 documented pregnancies. Only 9.1% (n=2) disclosed their HIV status to all their sexual partners, 18.2%(n=4) to some, 22.7%(n=5) to none, with 50.0%(n=11) unknown. Half of the sexually active youth (57.1%; n=12) had a HIV RNA viral load < 1000 copies/mL and 42.9%(n=9) had a viral load >1000 copies/mL.

CONCLUSIONS
One third of the perinatally infected adolescents in our study were reported to be sexually active with a median age of sexual debut of 15.6 years. Most perinatally HIV-infected adolescents did not disclose their HIV status to their sexual partners. Significant proportion of the patients had elevated viral load placing their partners at risk for transmission of HIV. Further studies are necessary to develop interventions to increase sexual educations and safe sex and reproductive health practices among perinatally HIV-infected youth.
Determining the rates of infection-related outcomes and the effectiveness of different screening strategies in patients who have undergone mandatory MRSA nasal carriage screening at San Francisco General Hospital

Methicillin-Resistant Staphylococcus aureus (MRSA) is an important pathogen in both community and nosocomial infections. MRSA infections are not only common and costly in terms of morbidity and mortality but also expensive to treat. In January of 2009 the California state legislature passed Nile’s law, which mandates hospitals to screen certain patients for MRSA within 24 hours of admission. Our research seeks to define the rates of infection-related outcomes in a cohort of subjects who have undergone mandatory MRSA screening and to compare the effectiveness of screening strategies in identifying those who might benefit from an effective intervention.

This study is a historical case-control study of 3755 adult patients who were admitted to San Francisco General Hospital and underwent MRSA nasal carriage screening between February 1, 2009 and June 1, 2011. Outcomes that were measured include demographics, index and recurrent nasal carriage information, microbiological history, and risk based on a Charlson co-morbidity score. Results showed that most who swabbed positive were males (71%). The most prevalent ethnicity that swabbed positive was Whites (42%), African Americans (30%), and Hispanics (11%). With regards to infection outcomes, 8% of those who swabbed positive went on to develop a MRSA infection within 90 days of the swab while only 1% of those who swabbed negative went on to develop an MRSA infection in that same time frame.

Further data analysis is pending and we plan to define subpopulations and comorbidities that may be suitable for mandatory screening, and to define what kind of screening, if any, may be appropriate for these sub-classifications. It is also in our preview to define the molecular epidemiology of carriage isolates of MRSA. Our hope is to ultimately apply clinical, demographical, and epidemiological parameters to develop more targeted screening.
Myeloid-derived suppressor cells protect islet transplants by B7-H1 mediated enhancement of T regulatory cells

BACKGROUND
Side effects of lifetime immunosuppression for cell transplants often outweigh the benefits; therefore, induction of transplant tolerance is needed. We have shown that cotransplantation with myeloid-derived suppressor cells (MDSC) effectively protect islet allografts from rejection without requirement of immunosuppression. This study was to investigate the underlying mechanisms.

METHODS
MDSC were generated by addition of hepatic stellate cells from various stain mice into dendritic cell (DC) culture. The quality of MDSC was monitored by phenotype and function analyses. MDSC mixed with islet allografts were transplanted into diabetic recipients. T-cell response was analyzed after transplantation by using flow and histochemical analyses, and was compared with islet alone and islet/DC transplant groups. B7-H1 knockout mice were used to determine the role of B7-H1 on MDSC in regulation of T-cell response.

RESULTS
Cotransplantation with MDSC (not DC) effectively protected islet allografts without requirement of immunosuppression. This is associated with attenuation of CD8 T cells in the grafts and marked expansion of regulatory T (Treg) cells, which contributed to MDSC-induced T-cell hyporesponsiveness. Antigen-specific Treg cells were prone to accumulate in lymphoid organs close to the grafts. Both in vitro and in vivo data demonstrated that B7-H1 was absolutely required for MDSC to exert immune regulatory activity and induction of Treg cells.

CONCLUSION
The described approach holds great clinical application potential and may overcome the limitation of requiring chronic administration of immunosuppression in cell transplants. Understanding the underlying mechanisms will facilitate the development of this novel therapeutic strategy.
Programmed death receptor-1 (PD-1) blockade in patients as a novel immunotherapeutic strategy to treat Hepatitis B

BACKGROUND

Globally, about 350 million people live with chronic Hepatitis B (CHB). The differential treatment responses observed between immunomodulatory (Interferon) and nucleoside analog Hepatitis B (HBV) drugs suggest that an immune mediated mechanism is essential for clearance of HBV and development of protective immunity. This study’s aim was to determine the effect of anti-HBV therapy on the immunoregulatory pathways associated with HBV viral response, in order to develop novel therapeutic strategies.

METHODS

In a National Institute of Allergy and Infectious Diseases IRB-approved prospective, double-blind, randomized placebo controlled trial, HBV infected patients with HIV were treated with adefovir 10 mg daily (n=8) or placebo for 48 weeks (n=3). HBV mono-infected patients enrolled in an open label study received adefovir for 48 weeks (n=5). Immunophenotyping, functional studies (cytokine secreting CD8+ T-cells specific to pooled overlapping HBV peptides), and effect of PD-1 blockade (programmed death receptor-1 blockade using anti-PD-1 and anti-PD-L1/L2 antibodies) were assessed at multiple time points using peripheral blood mononuclear cells. FoxP3 and PD-1 expression in liver biopsies performed pre- and post-treatment were determined by immunohistochemistry. Statistical analyses were performed using ANOVA and t-tests with corrections for multiple comparisons. R-values were calculated using Pearson correlation coefficient.

RESULTS

Peripheral expansion of T-regulatory cells (T-regs) correlated with HBV viral load (HBV mono-infected r=0.49, p=0.03; HBV/HIV co-infected r=0.67, p=0.01.). In both HBV mono-infected and HBV/ HIV co-infected patients, T-regs suppress HBV-specific CD8+ T-cell responses at baseline (p<0.0001). Control of HBV replication with adefovir results in a decrease in T-regs and increase in HBV-specific immunity as measured by increased cytokine secreting CD8+ T-cells at 48 weeks (p<0.001). This however, did not result in development of protective immunity [HBsAg seroconversion (0%) or HBeAg seroconversion (6%)].

PD-1 expressing T-regs in the periphery and liver decreased on adefovir therapy, but still remained high in both HBV mono-infected and HIV/HBV co-infected CHB patients (24 ± 5% and 39 ± 4% peripheral PD- 1+ T-regs at 48 weeks in HBV and HIV/HBV infected patients respectively; p<0.01). PD-1 blockade was effective in vitro in boosting HBV-specific peripheral immunity in both HBV mono-infected and HIV/HBV co-infected patients (p<0.005).

CONCLUSIONS

Chronic Hepatitis B is associated with increased PD-1+ T-regs, which suppress HBV-specific immunity. Blockade of PD-1 is likely to boost HBV immunity and enhance treatment response. Our study suggests that therapies involving PD-1 blockade in combination with directly acting antivirals may be an effective strategy to enhance development of protective immunity in CHB.
Germline Transgenesis and Insertional Mutagenesis in Schistosoma mansoni Mediated by Murine Leukemia Virus

BACKGROUND

Functional studies will facilitate the characterization of the role and essentiality of newly available genome sequences of the major human schistosomes, Schistosoma mansoni, S. japonicum and S. haematobium. To develop transgenesis as a functional approach for these pathogens, we previously demonstrated that pseudotyped murine leukemia virus (MLV) can transduce schistosomes leading to chromosomal integration of reporter transgenes and short hairpin RNA cassettes.

METHODS AND RESULTS

Here we investigated vertical transmission of transgenes through intra-snail stages of S. mansoni. Although MLV infection of schistosome eggs from mouse livers was efficient in terms of snail infectivity, >10-fold higher transgene copy numbers were seen in cercariae derived from in vitro laid eggs (IVLE). Targeting IVLE with transgenes increased the likelihood of transducing germline cells. High-throughput sequencing of genomic DNA from schistosome populations exposed to MLV revealed widespread and random insertion of transgenes throughout the genome, along each of the autosomes, chromosomes 1 to 7, and the sex chromosomes Z and W, confirming the utility of this approach for insertional mutagenesis. After infecting snails with miracidia from eggs transduced by MLV, sequencing of genomic DNA from cercariae released from the snails also revealed the presence of transgenes, demonstrating that transgenes had been transmitted through the asexual developmental cycle, and thereby confirming germline transgenesis. In addition, the germline-transmitted transgene encoding neomycin phosphotransferase rescued cultured schistosomules from toxicity of the antibiotic G418.

CONCLUSIONS

These findings provide the first report of wide-scale, random insertional mutagenesis of chromosomes and of germline transmission of a transgene in schistosomes. Transgenic lines of schistosomes expressing antibiotic resistance could advance functional genomics for these significant human pathogens.
CD47 (integrin-associated protein) is a ubiquitous transmembrane receptor. Interactions of CD47 with its ligand thrombospondin-1 and its counter-receptor signal regulatory protein-α (SIRP-α) on phagocytes have been implicated in numerous innate immunological functions. Recently, we discovered that CD47 knockout mice (CD47-/-) challenged with systemic candidiasis exhibited increased inflammatory responses and poorer survival than infected wild type controls. Kidney is the major site of colonization for disseminated candidiasis, and we observed more inflammation in kidneys of CD47-/- mice than wild type. To understand the molecular basis of this inflammatory response we examined the inflammasome. NLRP3 and caspase-1 mRNA expression and mature caspase-1 and IL-1β protein levels were significantly upregulated in kidneys of CD47-/- mice infected with Candida albicans compared to wild type controls. In vitro knockdown of CD47 in human THP1 cells increased mature caspase-1 and IL-1β protein responses to lipopolysaccharide (LPS), a known NLRP3 inducer, compared to vehicle control. Lastly, cells treated with thrombospondin-1 and other CD47 ligands and stimulated with LPS have significantly higher mature caspase-1 and IL-1β protein levels than unstimulated controls. These data provide evidence that in the absence of CD47 individuals are more susceptible to NLRP3-dependent inflammation providing a molecular rationale for our previous observations.
Platelet-Induced Splenocyte Apoptosis during Sepsis is Inhibited by GPIIb/IIIa Blockade

BACKGROUND
End-organ apoptosis is considered a diagnostic hallmark of progressive sepsis and multi-organ dysfunction syndrome (MODS). Platelets have been shown to accumulate in many commonly affected end-organs (e.g. spleen and lung) during sepsis. We previously reported an increase in platelet granzyme B (GzmB) expression during experimental sepsis that co-localized with platelet aggregates and induced apoptosis in both splenic and lung tissue. Our subsequent work confirmed that this platelet-induced splenocyte apoptosis is dependent upon direct platelet – target cell contact.

OBJECTIVE
To determine if known anti-platelet aggregation agents inhibit platelet-induced splenocyte apoptosis ex vivo.

METHODS
We used a cecal ligation and puncture (CLP) model of murine sepsis and our previously published platelet:splenocyte co-incubation assay. Anti-platelet agents tested included a GpIIb/IIIa inhibitor (i.e. eptifibatide) and an antibody with blocking activity against the platelet cell adhesion molecule P-Selectin (i.e. CD62P). Splenocyte apoptosis was measured using TUNEL-based assays and flow cytometry.

RESULTS
Ex vivo co-incubation of septic platelets and healthy splenocytes in the presence of eptifibatide significantly decreased apoptosis (i.e. TUNEL staining) in splenocytes (overall and among CD4+ populations) as compared to co-incubation with non-treated septic platelets (means±SEM [overall] = 66.5±10.6% reduction, P=0.008; means±SEM [CD4+] = 85±20.7% reduction, P=0.026). When septic platelets were co-incubated in the presence of blocking anti-CD62P antibody, there was no statistical difference from baseline levels of apoptosis.

CONCLUSIONS
Inhibition of aggregation/contact between platelets and splenocytes with eptifibatide decreased levels of splenocyte apoptosis ex vivo. If eptifibatide inhibition of apoptosis is translatable to in vivo studies, it may represent a novel therapeutic option in the treatment of sepsis and MODS.
Hookworms are intestinal parasitic nematodes that establish chronic infection in their hosts. The parasitic hookworm immunosuppresses the host through the excretory / secretory products. One of the most abundant proteins, a putative tissue inhibitor of metalloproteases, AcTMP1, has immunosuppressive role, but its biochemical mechanism for immunosuppression has not been determined. AcTMP1 is a member of the TIMP-like clan, a group of protein families comprised of the tissue inhibitors of metalloproteases (TIMPS), the Netrins, and the C345C domain found in complement proteins. Although the TIMP-like clan proteins have a conserved fold, their functions are varied. Our goal was to identify a biochemical function for AcTMP1 using functional genomic approaches.

To this end, a recombinant AcTMP1 was synthesized and its activity was tested against metalloproteases, complement lysis, and protein binding using in vitro assays. Recombinant AcTMP1 inhibits some matrix metalloproteases in a dose-dependent manner. A truncated version of rAcTMP1 missing the N-terminal CXC motif was inactive, confirming that AcTMP1 is a tissue inhibitor of metalloproteases and uses the classic cysteine-switch inhibition mechanism. The IC50 of rAcTMP1 with MMP-14 is 100 nM, ten-fold less potent compared with human TIMP2, a natural inhibitor of MMP-14. rAcTMP1 had no anticomplement activity, and like the human TIMP2, binds integrin.

These results suggest that the hookworm AcTMP1 has TIMP and Netrin-like activities. AcTMP1 may be exerting its immunosuppressive effect by binding integrin in the surface of leukocytes, preventing their extravasation to the site of hookworm infection, and potentially modulating their cytokines production.
INSTITUTE FOR BIOMEDICAL SCIENCES

Innate Helper 2 Cells in Human Peripheral Blood: A Role in Filarial Immunity?

BACKGROUND

The innate immune cells and factors responsible for directing T cells towards a Th1 response are well characterized. However, the factors and cells involved in initiating a Th2 response are not as well understood. Recently, several groups have demonstrated that a group of innate cells that respond to IL-25 and IL-33 and produce the Th2 cytokines IL-13 and IL-5 may play an important role in Th2 cell development. Deemed innate helper type 2 cells (IH2 cells), these cells were identified in mice and found to be crucial for initiating the immune response to intestinal helminths. The purpose of our studies was to determine if these IH2 cells exist in humans and whether IH2 cells play a role in the immune response to filarial parasites in terms of initiating a Th2 response.

METHODS

Whole blood from patients with active lymphatic filariasis and filarial-uninfected controls from India was lysed, fixed and cryopreserved. Following thawing, the cells were stained with a multicolor cocktail of antibodies. The number of IH2 cells (lineage-, CD45+, cKit+ and IL-7Ra+) were quantified in each patient group using flow cytometry and cell numbers compared between normal and infected patients.

RESULTS

IH2 cells were found in whole blood of both normal and filarial-infected patients. There was an increase (p= 0.3) in the percentage of IH2 cells in infected patients.

CONCLUSIONS

IH2 cells were found to be present in peripheral blood in humans but do not seem expanded in patent filarial infection. Currently, studies are underway to purify this cell population from peripheral blood and use the sorted cells to determine the function of IH2 cells at homeostasis and in the a Th2 dominated immune environment such as filarial infection.

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Repression of MUC5AC Gene Expression by the Δ 9,11 Compound, VBP15, in Human Lung Epithelial Cells

BACKGROUND
Glucocorticoids are commonly used drugs for a variety of diseases, including asthma. Because adverse side effects are observed in patients on long-term glucocorticoid treatment, alternative drugs are actively sought. One example are Δ 9, 11 glucocorticoid analogues, also known as VBP compounds. VBP compounds have been shown to activate nuclear translocation of GR although they do not induce GR/GRE-mediated transcriptional upregulation, but rather inhibit TNFα-induced NFκB signaling. Thus, they have the potential to maintain the therapeutic effects but lack the harmful side effects of long-term steroid therapy. Previous studies from our lab have shown that the glucocorticoid Dexamethasone (Dex), transcriptionally represses expression of the MUC5AC mucin gene in lung epithelial cells in vitro and that Dex-activated GR binds to two GRE cis-sites in the MUC5AC promoter. Overproduction of mucins, specifically MUC5AC and MUC5B, contributes to morbidity and mortality in lung diseases; therefore, we investigated the ability of VBP15 to modulate mucin gene expression.

METHODS
VBP15 or Dex were exposed to A549 cells, a human lung epithelial cell line; Expression levels of MUC5AC, and β-actin mRNA were determined by SYBR Green RT-PCR. Cells were pre-exposed to RU486, a GR antagonist, and then to VBP15 to determine the effect of RU486 on VBP15-induced MUC5AC repression. Immunofluorescence was utilized to determine whether GR translocates to the nucleus following VBP15 exposure over time.

RESULTS
VBP15 reduced MUC5AC mRNA abundance in a dose- and time-dependent manner. Repression occurred optimally at a concentration of 1μM of VBP15 and between 6 and 18 hours of exposure. Data showed that both the VBP15- and Dex-induced repression of the MUC5AC gene was completely abrogated in the presence of 1μM RU486. Immunofluorescence demonstrated that VBP15, similarly to Dex, induced nuclear translocation of GR within 0.5 hours in A549 cells and within 1 hour in human differentiated nasal epithelial cells.

CONCLUSIONS
These data demonstrated that VBP15 can repress MUC5AC gene expression and that this process requires GR. Preliminary studies indicated that VBP15 likewise repressed gene expression of the MUC5B mucin gene and that VBP15 also represses MUC5AC and MUC5B gene expression in primary differentiated human bronchial epithelial cells. Future experiments will focus on mechanistic studies to determine how VBP15 represses gene expression of mucins. VBP15 may be a useful drug if its potential to reduce mucin overproduction in the lungs of patients with airway diseases without the harmful side effects observed in long-term glucocorticoid treatment is fulfilled.
Pott’s Disease: An uncommon cause of back pain

A 24 year old otherwise healthy man presented to clinic with new onset, severe 9/10 back pain in the spinal and para-spinal lumbar region, which radiated into the right buttck, and right posterior thigh. It was aching in character, and lasted up to several hours a day. Movement, in particular, back extension and hip flexion, exacerbated the pain. Leaning forward while ambulating alleviated the pain. It improved with rest, but would not resolve completely, and at times the pain awakened him from sleep. He denied injury, radicular symptoms, or neurologic deficits. He took no medications, had no allergies, and no family history of illness. Social history was significant for immigrating to the US from India at the age of 6. Review of systems was otherwise negative. Vital signs were unremarkable. Physical exam revealed tenderness to palpation along the lumbar paraspinal muscles bilaterally, and spinal tenderness at several points distal to L2. Strength, sensation and reflexes were normal. He was treated for a presumed back strain with ibuprofen and cyclobenzaprine. This provided relief, however, over the course of a year, he continued to suffer bouts of back pain. He presented to the emergency room, where a spinal MRI showed multiple, noncontiguous abscesses in his thoracic and lumbar vertebrae. There was also an 8 cm lesion in his right psoas muscle. PPD and interferon gold tests were positive, and aspiration of the psoas abscess showed acid fast bacilli. Culture grew mycobacterium tuberculosis.

Lumbar muscle strain is the most common etiology of back pain in a young adult, and accounts for more than 90% of cases. More serious causes of spondylar disease should be considered for intractable pain that fails to respond to conservative treatment, pain that occurs at night while resting, accompanied by systemic symptoms or neurologic deficits, or if there is spinal tenderness on exam. 11,182 TB cases of active tuberculosis were reported in the United States in 2010. Tuberculous spondylitis (Pott’s Disease) is an uncommon form of active tuberculosis and occurs in about 1% cases. It is usually seen in older children and young adults from TB endemic countries. Spinal tuberculosis is the result of either hematogenous spread, lymphatic spread, or extension of contiguous disease from an extraspinal source. Lesions are most commonly seen in the lower thoracic and upper lumbar spine, and can spread to the intervertebral disc, adjacent vertebrae, distant vertebrae, epidural space, psoas muscle, and the posterior iliac crest. Physical exam often shows spinal tenderness. Advanced disease can lead to muscle weakness and paralysis. Systemic tuberculosis symptoms are often absent, and Xrays can miss early lesions. MRI is the most sensitive in identifying early disease and is the standard for evaluating disk-space infection, osteomyelitis of the spine, and extension of disease into soft tissues. Tuberculomas on MRI show thin, smooth enhancement of the abscess wall, whereas pyogenic spondylitis is characterized by thick and irregular enhancement of the abscess wall. The diagnosis of spinal TB is confirmed with an AFB positive aspirate. Treatment is with antimycobacterial agents.
New Onset Focal Epilepsy in a 52 Year Old Woman with a Frontal Dysembryoplastic Neuroepithelial Tumor Presenting as Neurocysticercosis is Cured after Complete Resection: A Case Study

OBJECTIVE

To report a case of Dysembryoplastic neuroepithelial tumor in an older adult who presented with new onset epilepsy and a brain MRI consistent with neurocysticercosis who was later cured and diagnosed after total resection of the lesion.

BACKGROUND

Dysembryoplastic neuroepithelial tumor (DNT) is commonly associated with drug-resistant epilepsy beginning in childhood. While DNTs may occur in the adult population, literature reports of DNT outside childhood and adolescence remain relatively rare.

DESIGN

Case Study

RESULTS

In this case study we describe a 52 year old woman presenting with new-onset complex focal seizures whose brain MRI revealed findings consistent with neurocysticercosis. However, after a course of anthelmintic treatment, steroids, and initiation of antiepileptic medication, the patient's epilepsy continued, and the cystic lesion remained unchanged upon repeat imaging. Complete neurosurgical resection of the lesion led to resolution of the epilepsy and allowed for the pathological diagnosis of DNT. The roles of radiologic and pathologic study are discussed with respect to achieving a final diagnosis.

CONCLUSIONS

Unusual seizure-associated tumors more commonly seen in children should be considered in the differential diagnosis of adults presenting with epilepsy attributed to parasitic cysts.
Identification and characterization of Lman1 in retinal degeneration

BACKGROUND

The process of vision begins at the photoreceptors in the retina, which provide nearly 30% of the sensory input to the brain. Neurodegenerative blinding diseases due to genetic defects that cause abnormal differentiation or homeostasis of retinal photoreceptors are the primary cause of visual impairment in diseases of the retina. The neural retina leucine zipper (NRL) transcription factor is a key regulator of rod photoreceptor differentiation and homeostasis. NRL functions as a molecular switch to produce rod photoreceptors from post-mitotic retinal precursor cells. Lman1 encodes ERGIC-53, a protein mediating the transfer of a subpopulation of glycoproteins from the ER to the Golgi complex. ERGIC-53 also functions in glycoprotein quality control and it is ubiquitously expressed. We identified the Lman1 gene as a direct transcriptional target of NRL. To identify the potential role of Lman1 in retinal degeneration, we investigated its regulation and function in rod photoreceptors using Lman1 knockout mice.

METHODS

Chromatin immunoprecipitation followed by real-time quantitative polymerase chain reaction (ChIP-qPCR) and enhancer analysis of the Lman1 enhancer element were used to validate the interaction between NRL and Lman1 promoter sequences. ChIP-qPCR and enhancer analysis detected the Lman1 promoter as a direct target of NRL. Physiologic relevance of Lman1 in the retina was tested using immunohistochemistry (IHC) in Lman1 knockout mice. Retinas were collected from Lman1-/- mice at 2 months and 6 months of age. The retinas were sectioned, and IHC was performed against the Golgi markers GM130 and Grasp65, glial marker GFAP, and the rod photoreceptor visual pigment rhodopsin.

RESULTS

IHC showed reduction in Grasp65 and rhodopsin in 2 month and 6 month old Lman1-/- mice compared to WT, whereas no significant difference in GFAP was observed. IHC against GM130 also showed significant reduction in 2 month old Lman1-/- compared to WT.

CONCLUSIONS

Our results suggest that Lman1 has an important role in rod photoreceptor development and homeostasis. Function tests will be conducted to evaluate the retina of Lman1-/- mice through light damage and electroretinography analyses.
Preliminary analysis of assessing complementary and alternative medicine use, effectiveness, interest and perceived barriers to use in patients with pain

INTRODUCTION

Complementary and alternative medicine (CAM) has become more widely used by patients within the United States, with one national survey demonstrating an increase of approximately 8% of patients using CAM from 1990-1997. (Eisenberg, 1998) Many patients seek care simultaneously from physicians and alternative practitioners. (Muhajarine, 2000) Patients with chronic pain are interested in trying CAM therapies (Sherman, 2004), but barriers to CAM usage are not fully understood. (Gaul, 2011) We proposed a survey to study the demographics of the chronic pain population in addition to usage, interest, communication, effectiveness of CAM and perceived barriers to utilizing CAM therapy.

MATERIALS AND METHODS

DESIGN

Cross-sectional survey.

PARTICIPANTS

Patients who see one of three physicians or a physician assistant at a chronic pain center. A total of 85 patients completed the survey.

RESULTS

Patients primarily had previously tried massage (24.7%), movement therapy (20.0%), acupuncture (20%), chiropractory (17.6%), deep breathing (16.5%) and yoga (16.5%). Sixty-five percent of patients who had tried one or more CAM therapies discussed their use with a pain physician. 60.6% of patients were interested in trying CAM for pain relief. 38.8% of patients had been asked about their interest in CAM by a physician, while 61.2% had not been. Patients identified perceived barriers to CAM usage as lack of knowledge about CAM (29.5%) high expense (25.0%), lack of time (22.7%) and providers (11.4%) and fear of pain (11.4%).

CONCLUSIONS

Patients with chronic pain are interested in CAM and have tried CAM therapies to decrease their pain, and some barriers to CAM utilization are identifiable. Interest in CAM is high, although pain physicians do not routinely ask about or discuss CAM. While the results of this survey are preliminary, we hope to collect a total of 150 surveys to have a better understanding of the true impact of this study.
Neuroscience

School of Medicine and Health Sciences

Tyrosine Kinase Activity Contributes to the Inflammation-Induced Shift in Spinal GABA-A Receptor Signaling in the Rat

Introduction

Previous data indicates that persistent inflammation drives a shift in spinal \(\gamma\)-aminobutyric acid receptor type A (GABAA) signaling that contrasts the normal analgesia associated with exogenous application of the GABAA receptor selective agonist muscimol. Instead, the agonist exacerbates inflammatory hypersensitivity. In vitro experiments suggest that an increase in GABAA current plays a prominent role in this shift in the presence of persistent inflammation. The increase in GABAA current is mediated by a relative increase in tyrosine kinase activity. This behavioral pharmacological study determines the contribution of an increase in tyrosine kinase activity to the inflammation-induced shift in spinal GABAA signaling.

Methods

Rats received chronic indwelling intrathecal catheters targeted to the lumbar enlargement and randomized to one of four groups defined by the presence or absence of persistent inflammation and whether they received an active (genistein 0.1 mg) or inactive (genistin 0.1 mg) tyrosine kinase inhibitor. Rats were studied three days after induction of persistent inflammation with an injection of complete Freund’s adjuvant (CFA, 100 \(\mu\)l) into the left hindpaw. Mechanical nociceptive threshold was determined with an electronic von Frey device where a rigid tip (~1 mm) was applied to the dorsal surface of the hindpaw, before and 20 min after IT administration of genistein or genistin. Rats then received another IT injection of muscimol (0.1 \(\mu\)g) and mechanical threshold was determined 10 minutes later.

Results

CFA injection resulted in a significant decrease in mechanical threshold. There was no significant influence of genistein on nociceptive threshold in naïve or inflamed rats. However, there was a significant interaction between inflammation and kinase inhibitor treatment on the response to muscimol such that in the absence of inflammation and kinase inhibitor, muscimol elevated mechanical threshold, in the presence of inflammation but absence of kinase inhibitor, muscimol decreased mechanical threshold, while in the presence of inflammation and kinase inhibitor, muscimol increased nociceptive threshold.

Conclusion

Persistent changes in relative levels of tyrosine kinase activity not only provide a sensitive way to dynamically regulate spinal nociceptive signaling, but a viable target for the development of novel therapeutic interventions for the treatment of inflammatory pain. Given recent results suggesting that the inflammation-induced shift in spinal GABAA signaling may have deleterious consequences for patients undergoing surgical interventions if the anesthetics employed during the procedure are GABAA preferring, (Boegel et al., 2011), the perioperative setting may be one context in which inhibition of tyrosine kinase activity may be useful.
BACKGROUND

There is debate whether enlargement of the corpus callosum in patients with NF-1 is congenital versus acquired and whether it represents increased number of fibers versus thicker myelin sheaths or other explanations. [Wignall] The goal of our study was to compare DTI parameters from pediatric NF-1 patients with enlarged corpus callosum to normal sized corpus callosum in matched controls without a diagnosis of NF-1.

METHODS

Retrospective study. Patients and matched controls were consecutively selected from a database of the NF-1 clinic and the PACS system at our institution. The corpus callosum to skull ratio was measured for all patients and controls on the midline image of the sagittal T1 SE or SPGR sequence. DTI images were analyzed using DTIstudio [Jiang] and manual regions of interest (ROI) over the entire corpus callosum. Radial and axial diffusivity, apparent diffusion coefficient (ADC), and fractional anisotropy (FA) were documented in all subjects.

RESULTS

15 NF-1 patients and 15 matched controls were analyzed. Most DTI parameters between NF-1 patients and controls were significantly different: axial diffusivity was lower in NF-1 (p=0.0002), FA was lower in NF-1 (p=0.0012), and radial diffusivity was higher in NF-1 (p=0.023). ADC was the only DTI measurement not significant (p=0.067).

DISCUSSION

Several explanations for the enlarged size of the corpus callosum in NF-1 patients have been proposed, including increase in the number of commissural fibers due to reduction in apoptosis, excessive myelination, increased extracellular fluid, myelinopathy associated with vacuolation or a combination of all four of those factors [Wignall]. Based on our DTI assessment we believe that decreased axial diffusivity in NF-1 patients indicates a larger amount of fibers in the corpus callosum that are not parallel. These may represent abnormal branches or unusual connections across the midline. Since axial diffusivity is the main arithmetical component in how FA is calculated, the fact the axial diffusivity is lower can also explain that FA is lower. The higher value for radial diffusivity may indicate increased interstitial space between axons- either thin myelin or thin axons or combination of both. These assumptions have to be viewed cautiously due to the small sample size in our study.

CONCLUSIONS

DTI is a promising imaging tool that can help further describe the pathophysiology that underlies corpus callosum enlargement in NF-1 patients. DTI analyses in larger patient populations will help solidify the data presented here and may affect alternative interpretations.
Prevalence of spondylololithesis in whiplash associated disorder

INTRODUCTION
Whiplash is a common injury after traumatic events, including motor vehicle accidents and falls. Patients with whiplash complain of pain and disability for years after the injury, and a large gap in knowledge exists for understanding the entirety of whiplash injury with respect to neck anatomy. (Rydevik, 2008)

A case-control study has investigated the existence of middle cervical segmental motion after whiplash injury compared to controls, and demonstrated more C3-C4, C4-C5 and C5-C6 motion in the injured population. (Kristjansson, 2003) Likewise, one case report has documented C2-C3 pseudosubluxation following whiplash. (Curtin, 2005) We retrospectively report the prevalence of cervical spondylololithsis over a two-year period in patients with a history of known whiplash injury.

MATERIALS AND METHODS
Study Design: Retrospective chart review as approved by the appropriate IRB.
Subjects: Twenty-three patients were identified as having a history of whiplash between May 2009 through June 2011. Corresponding neutral, flexion and extension cervical x-rays were examined and measured for affected cervical level and spondylolithesis.

RESULTS
All patients except for one had some element of spondylolithsis. The cervical levels primarily affected were C4-C5 (10 out of 23 patients) and C3-C4 (9 out of 23 patients). Other affected levels included C2-C3 and C5-C6. Spondylolithsis was most prevalent in the flexion and extension positions compared to the neutral position.

CONCLUSIONS
Out of the examined whiplash injured population, all except for one patient had evidence of spondylolithsis, primarily at the C4-C5 and C3-C4 levels. Further research is needed into investigating whether a correlation exists between the physical and radiographic findings of whiplash patients. Ideally, targeted therapy for the spondylolithsis found in whiplash patients would provide optimal care.
Perinatal SO2 exposure alters brainstem neurons that mediate autonomic control of heart rate

The World Health Organization estimates that 3 million individuals die annually due to the negative health effects associated with air pollution exposure. Sulfur dioxide (SO2) is an air pollutant released upon the burning of coal for electricity generation, and is strongly associated with cardiorespiratory disease. Epidemiological studies have shown SO2 exposure leads to an increase in resting heart rate and a decrease in heart rate variability. It has been hypothesized that these effects are caused by altered autonomic control of cardiovascular function, but the mechanism(s) responsible for these outcomes are unknown. Additionally, while these studies have focused on adult exposures, the Environmental Protection Agency (EPA) has stated that there is a lack of research addressing the health effects of prenatal and neonatal SO2 exposure. To address this question, a chamber was designed to expose pregnant Sprague-Dawley rats to 5 parts per million (ppm) SO2 for one hour daily during pregnancy and one week after giving birth. Parasympathetic activity was studied in neonatal rats (postnatal days 2-7) by identifying premotor cardioinhibitory vagal neurons (CVNs) in the nucleus ambiguus in an in vitro brainstem slice preparation retaining rhythmic respiratory activity. Individual CVNs were whole-cell patch clamped and isolated for spontaneous glutamatergic or inspiratory-related glycinergic or GABAergic neurotransmission. While inhibitory neurotransmission was unaltered, SO2 exposure significantly decreased glutamatergic neurotransmission to CVNs in an action potential-dependent manner. Additional results have shown that this effect is elicited by postnatal exposure to SO2 only. These findings suggest that a cellular target of SO2 exposure is a decreased excitatory neurotransmission to CVNs, causing decreased parasympathetic control of resting heart rate, tachycardia, and autonomic imbalance to the heart.
Endothelin-1 regulates Jagged/Notch signaling to inhibit remyelination

Multiple sclerosis (MS) results in demyelinated lesions throughout the central nervous system. In response to demyelination, oligodendrocyte progenitor cells (OPCs) repopulate the lesion and begin to differentiate into mature myelinating oligodendrocytes (OLs). Some lesions, however, fail to remyelinate for unknown reasons. Understanding the signaling mechanisms that control OPC differentiation in remyelinating lesions is essential for development of therapies aimed at promoting remyelination in MS patients. The Jagged1/Notch1 pathway has been previously shown to attenuate OPC development in demyelinated lesions. Here we show that the neuropeptide, endothelin-1 (ET-1), induces an upregulation of Jagged1 expression in cultured astrocytes, which is blocked by pan-endothelin-receptor (ET-R) antagonist PD142,893. We also show that ET-1 pre-treated astrocytes inhibit OPC differentiation in a co-culture system. To investigate the effects in vivo, we used focal injections of lysolecithin (LPC) into the mouse corpus callosum/cingulum to induce focal demyelination. In LPC-injected mice we found that ET-1 levels are upregulated near the lesion, and that ET-1 is expressed by astrocytes and endothelial cells at high levels at 3 and 7 days post lesion (dpl). In Western blot analysis of micro-dissected tissue we saw increases in ET-1 at 3 dpl, and a peak in Jagged1 expression at 7 dpl. We also saw increases in Notch intracellular cleaved domain (NICD) expression at 7dpl. Next, we investigated cell specific activation of Notch1 in demyelinated lesions using a transgenic Notch reporter mouse (TNR). We found that Notch1 signaling is activated in remyelinating lesions around 7 dpl, and that Notch1 is mainly activated in oligodendrocyte lineage cells (CC1+ and NG2+). To determine if ET-1 directly influenced Notch1 activation, we infused the ET-R pan-antagonist PD142,893 into the lesion following demyelination and found a decrease in the number of EGFP+ TNR cells. Finally, longer term infusion of ET-R antagonists led to increased numbers of CC1+ mature oligodendrocytes and increased levels of myelin basic protein (MBP) and CNP. Altogether these data show that ET-1 regulates Jagged1 expression in astrocytes, and that this leads to activation of Notch1 in demyelinated lesions. Activation of Notch1 in demyelinated lesions inhibits OPC differentiation and Notch is activated throughout the oligodendrocyte lineage, not just in OPCs. These data show that ET-1 is a major factor that modulates Notch1 signaling during remyelination to inhibit differentiation of oligodendrocytes, and to prevent remyelination. We find that ET-1 mediated inhibition of remyelination can be blocked using specific ET-R antagonists to promote remyelination. Supported by MS society grant #RG4019."
Photoexcitation of channelrhodopsin-2-expressing processes originating from the paraventricular nucleus of the hypothalamus evokes neurotransmitter release onto brainstem parasympathetic premotor cardiac vagal neurons

Descending projections from the paraventricular nucleus of the hypothalamus (PVN) play a major role in the autonomic nervous system control of cardiorespiratory function. PVN neurons have been shown to project to several brainstem sites, including nucleus ambiguus (NA), dorsomotor nucleus of the vagus (DMV), rostral ventrolateral medulla (RVLM) and nucleus of the solitary tract (NTS). While the role of the PVN in cardiovascular control is well documented, the role of the PVN in parasympathetic cardiovascular regulation is relatively unknown and has yet to be tested directly. In this study we examine the descending PVN projections to brainstem parasympathetic cardiac neurons by microinjecting different lentiviral vectors that drive channelrhodopsin-2-EYFP (ChR2-EYFP) fusion protein expression under a human synapsin1 promoter fragment into the PVN of the rat. In addition we employ the cre/lox transgenic mouse techniques to specifically express ChR2 in the PVN. Confocal microscopy analysis confirms close apposition of ChR2-EYFP fibers to identified cardiac vagal neurons (CVNs) in the NA and DMV. Functional assessment of synapses of PVN projections to CVNs using in vitro patch clamp electrophysiology and photoexcitation of ChR2 demonstrate the presence of a monosynaptic neurotransmission from the PVN to CVNs as photoexcitation of PVN presynaptic terminals evokes an excitatory current in DMV CVNs, mediated by AMPA and NMDA receptors. We will further explore how low and high frequency stimulation of this pathway affects synaptic plasticity of preautonomic PVN output to CVNs, as well as the role of PVN-specific neuropeptides, such as oxytocin and vasopressin, in the neurotransmission to CVNs. Our results provide evidence that PVN projections to the brainstem are not limited to sympathetic control, but also include a direct pathway from the PVN to CVNs to activate parasympathetic cardiac neurons.
Parasympathetic cardiac vagal neuron excitation by photostimulation of spinal trigeminal neuron pathways

The trigeminocardiac reflex is the most powerful autonomic reflex. Activation of this reflex pathway by airborne irritants or water, stimulates nasotrigeminal sensory fibers eliciting a pronounced bradycardia and increase in parasympathetic cardiac activity. Exaggeration of this response can be fatal, and has been implicated in various cardiorespiratory diseases such as sudden infant death syndrome (SIDS). Parasympathetic cardiac vagal neurons (CVNs) in the nucleus ambiguus (NA) play an integral role in mediating this reflex. Stimulation of trigeminal sensory afferents elicits a polysynaptic excitatory glutamatergic neurotransmission to CVNs. In this study we utilized a UV photo uncaging system to identify the neurons in the spinal trigeminal nucleus (sp5) that project to CVNs by sequential photostimulation of clusters and single sp5 neurons that elicit excitatory glutamatergic neurotransmission to CVNs. These areas and neurons were also identified by using a herpes simplex virus 1 expressing GFP injected into the nasal mucosa of neonatal rats, and, using 2 photon confocal microscopy, areas of the brainstem expressing GFP+ trigeminal sensory afferent fibers within sp5 were identified. Results indicate scattered neurons in the spinal trigeminal tract that receive sensory afferent synaptic terminals project to and excite CVNs. Further work is necessary to determine if these neurons are located diffusely or in discrete clusters within the sp5. Supported by NIH grants HL 59895, HL 72006 to DM and American Heart Association predoctoral fellowship to CG. CG is a predoctoral student in the Molecular Medicine Program of the Institute for Biomedical Sciences.
Models of Sleep Apnea

Patients with obstructive sleep apnea (OSA) experience intermittent cessations of breathing during sleep resulting in decreased arterial oxygen and increased carbon dioxide (CO2) levels. OSA is a major risk factor in the development of hypertension. While animal models have been developed and used to mimic OSA, in the majority of these models animals are exposed only to chronic intermittent hypoxia (CIH). When exposed to CIH the breathing rate of animals increases leading to decreased levels of arterial CO2, a result that is at odds with the increased arterial CO2 levels that occurs in patients during an apnea. In this study we developed an animal model of OSA that exposes 28 day old male rats to CIH and hypercapnia (CIH/H) for 7-10 days. To examine changes in the cardiovascular system, we implanted into the abdominal aorta a wireless transmitter that measures arterial and EKG signals. The effect and time course of cardiac and blood pressure changes that occur in response to CIH/H will be assessed. Furthermore, electrophysiological techniques will be used to access the effects of CIH/H on cardiac vagal neurons (CVNs) located in the nucleus ambiguus of the brainstem that generate parasympathetic activity to the heart. We hypothesize that CIH/H exposure in vivo will be an improved model of OSA and that it will also alter the firing properties of CVNs.
The extraocular muscles (EOM) that are responsible for moving the eyes are differentially susceptibility to neuromuscular diseases. Even in patients with far advanced amyotrophic lateral sclerosis and Duchenne muscular dystrophy, eye movements remain normal, while patients with myasthenia gravis may only have eye movement abnormalities. The Kaminski Laboratory has dedicated itself to evaluating the basic biological characteristics of EOM in order to further define the differential involvement of EOM by disease with the goal exploiting this understanding for therapeutic purposes. Our central hypothesis is that maintenance of the mature EOM phenotype relies upon cell autonomous and non-cell autonomous regulatory mechanisms that are both shared with, and divergent from, other skeletal muscles. Our presentation summarizes our work to date. We identified a unique genomic profile that differentiates the EOM from other skeletal muscle that indicated that the muscle is limited in intrinsic complement inhibitors that would make it susceptible to complement-mediated disorders, such as myasthenia gravis. In an evaluation of the Pitx2 transcriptional factor, we found that it controls genes critical for defining the EOM’s unique contractile characteristics, which include fatigue resistance and very rapid contraction. Such work points to the potential for informed genetic manipulation that could enhance muscle contraction. We have also discovered that the EOM fibers are supported by the specific characteristics of EOM-derived fibroblasts and have begun to define how manipulation of fibroblast properties may alter EOM. Rigorous definition of the EOM phenotype offers the opportunity to manipulate them in treatment of ocular motility disorders, such as strabismus, Graves ophthalmopathy, and traumatic injury.
Overexpression of Epidermal Growth Factor Receptor Prevents Cognitive Impairment in a Mouse Model of Premature Brain Injury

A leading cause of sustained cognitive and neurodevelopmental impairment in the pediatric and adult population is very premature birth (VPT; <32 weeks gestation). Advanced neuroimaging has identified continued abnormalities in several cerebral structures that reflect disturbances of key developmental processes during the perinatal period. There is clinical evidence that decreased white matter (WM) volume and increased WM injury in the temporal lobes contributes to the cognitive deficits in this population. We use a mouse model of chronic perinatal hypoxia (Hyp), where mice pups are reared under Hyp conditions from postnatal day (P)3-P11. This model mimics the disrupted pattern of brain development found in VPT infants. In our previous studies, we have demonstrated that Hyp results in: i) a significant reduction of subcortical WM mature oligodendrocyte lineage (OL) cells with recovery in cell number and protein expression by adulthood; and ii) significant sensori-motor deficits on WM-specific tasks. Overexpression of epidermal growth factor receptor (EGFR) in OL cells prevents WM loss and sensori-motor deficits. We hypothesize that preventing WM injury by overexpression of EGFR attenuates hippocampal-dependent learning and memory deficits. We used the CNP-EGFP (CNP) mice, where all OL cells express green fluorescent protein and the CNP-EGFP-hEGFR (CNP-hEGFR) mice, where human EGFR is overexpressed in all OL cells. The 4 groups assessed were: i) Normoxia (Nx) CNP; ii) Nx CNP-hEGFR; iii) Hyp CNP; and iv) Hyp CNP-hEGFR. Nx CNP compared to Nx CNP-hEGFR performed similarly in all behavioral paradigms tested. At P30 and P60, Hyp CNP mice demonstrated significant impairment of recognition and recall on the Novel Object Recognition (NOR) test at 3 and 6-hour delays compared to both Nx groups (p<0.01). However, Hyp CNP-hEGFR mice performance was comparable to the Nx group (p>0.1) and significantly better than the Hyp CNP group (p<0.05). Using the Y-maze to assess spatial recognition at P30 and P60, we found that the Hyp CNP group performed significantly worse than the Nx group at a 1-hour delay (p<0.05), but Hyp CNP-hEGFR performance did not differ from the Nx group (p>0.1). Currently, we are characterizing OL cell populations, the expression of mature markers of myelination and axon cytoskeletal proteins in the hippocampus. Our findings provide evidence that preventing perinatal WM injury during developmental myelination prevents cognitive impairment.
Use of MR Spectroscopy in detecting biochemical markers used for prognosis in patients with partial ornithine transcarbamylase deficiency

BACKGROUND

Urea Cycle Disorders (UCD) represent a group of rare inborn errors of metabolism that result from single gene defects in the detoxification steps involved in clearing urea in the form of ammonia. These disorders are inherited as autosomal recessive traits, except for ornithine transcarbamoylase deficiency (OTCD), which is X-linked. Presentation of this disease involves hyperammonemic (HA) episodes that lead to a decrease in white matter structure, affecting cognitive and executive function. Children with partial defects suffer from intellectual and neurological deficits as the number of HA episodes increase in frequency and severity.

OBJECTIVE

H1 Magnetic Resonance Spectroscopy (MRS) was utilized to study patients with partial defects to find the correlations between two sets of parameters. The first set included a group of metabolites that were visible in different parts of the cortex. Myo-inositol (mI, a brain fluid stabilizer), glutamate (Glu, a primary marker of cognitive function), and glycerylphosphorylcholine (GPC, an acetylcholine precursor thought to indicate cognitive status). The other parameter to which to compare the metabolites to was the performance IQ which was a series of questions based on gathering a simple cognitive baseline.

METHODS

Nineteen adults with partial OTCD and 18 adult control subjects ages 19-59 years participated. MR spectroscopy was performed by using a 3T whole-body scanner. Fat and water was suppressed in order to make the metabolites more visible on the spectrum.

CONCLUSIONS

A high mI and GPC correlated with a statistically significant increase in pIQ while a high Glu correlated with a statistically significant decrease in pIQ. These results lend to the hypothesis that mI served as a protective factor in hyperammonemic episodes as well as GPC. Understanding the neurochemical basis for cognitive impairment is important in elucidating the mechanisms underlying pathologic outcomes and identifying relationships to prognostic markers of brain function.
How is language lateralization affected by clinical factors in patients with left hemispheric epilepsy?

OBJECTIVE
We aimed to determine the differences in lateralization induced by reading and listening paradigms, and whether early seizure onset would cause a higher incidence of atypical reading dominance due to the late development of this skill.

METHODS
101 patients with left focal epilepsy (mean age 23.2 years, range 8-50 years) and 24 normal controls (mean age 29.2 years, range 21-56 years) performed both reading stories and listening to stories tasks while activation was measured by 3T BOLD fMRI. Language activation patterns were characterized using region of interest laterality indices: Wernicke's area (WA), inferior frontal gyrus (IFG), and middle frontal gyrus (MFG). Language dominance was deemed left, right, or bilateral (LI \geq 0.20 atypical).

RESULTS
Reading was found to cause stronger left lateralization than listening in the middle frontal gyrus (t=-2.99, p=.003). Controls were more left lateralized than patients during the listening task at Wernicke's area (t=4.41, p=.00; \chi^2=5.19, p=.023) and middle frontal gyrus (t=3.25, p=.002; \gamma^2=8.29, p=.004), and during the reading task at Wernicke's area (t=2.38, p=.021). Patients with early seizure onset had a greater percent of atypical lateralization than patients with late seizure onset during the reading task at Wernicke's area (t=-2.03, p=.045; \chi^2=5.50, p=.019). Patients had significantly weaker left lateralization than controls in certain ROIs, and this was not dependent on MRI pathology. Early age of seizure onset correlated with a higher incidence of atypical lateralization during the reading task, which would indicate that the late development of reading skills and the early onset of brain disturbances cause a reorganization of reading networks.

CONCLUSIONS
The importance of understanding how reading networks develop with age and may be altered due to stressors will help us to further understand how the brain assigns roles within the language network, and possibly predict how reading networks may reorganize in epilepsy patients.
Delayed development of pyramidal neuron morphology in the prefrontal cortex of the chimpanzee: a Golgi study

Pyramidal neurons of the adult primate neocortex exhibit regional differences in morphology, showing greatest dendritic length and spine numbers in the prefrontal cortex, with less complex dendritic systems in other cortical regions. Comparative examination of maturational markers (e.g., synaptic density, dendrite length and spine numbers) in the neonatal neocortex suggests that different mechanisms characterize the development of regional specializations in humans and macaque monkeys. The prefrontal cortex of human neonates is not only characterized by neurons with the least complex dendritic arbors, but it also reaches maturity later than other regions. In monkeys, by contrast, adult-like differences between the prefrontal cortex and other areas are already present in newborns, and regional development occurs isochronously. While considerable research has been conducted on monkeys, little is known regarding cortical development in the great apes, the group of primates that comprise our closest living relatives. To investigate whether chimpanzees display human-like regional heterogeneity in the maturation of cortical pyramidal neurons, we used a rapid Golgi technique to examine dendritic tree morphology in areas BA10 (prefrontal), BA18 (visual association), BA4 (primary motor), and BA3 (primary somatosensory) in seven adult and seven infant and juvenile chimpanzees. Ten neurons per region per individual were selected and manually traced using a Neulucida computer-assisted microscopy system (MBF Bioscience). Complexity of neuronal morphology was quantified by six measures: 1) soma cell area 2) dendritic length 3) dendritic segment number 4) dendritic segment mean length 5) spine number and 6) spine density. Results demonstrated that, similar to other primates, pyramidal neurons of adult chimpanzees have greater dendritic length and more spines in the prefrontal cortex (BA10). Notably, in contrast to previous observations in monkeys, but similar to humans, neurons in the infant chimpanzee prefrontal cortex (BA10) displayed the least complex dendritic/spine systems. These findings suggest that the evolution of a cortical developmental pattern characterized by maturational delay of prefrontal neurons occurred at some point prior to the split between humans and chimpanzees. Accordingly, such a unique developmental profile of the cerebral cortex might have been important for the evolution of cognitive abilities in the ape lineage leading to humans.
CHILDREN’S NATIONAL MEDICAL CENTER

The Impact of a Nutritional Supplement on Metabolic Health in an Inner City Child-Parent Intervention

BACKGROUND

Nutritional deficiencies are prevalent in inner city children and their families and contribute to the disproportionate burden of obesity and cardiometabolic disease for complex reasons. Overcoming barriers to healthy lifestyle change may require a nutritional reset of the metabolome.

OBJECTIVE

To determine whether twice daily intake of an inexpensive, low-calorie, high-fiber, fruit-based nutrient-dense bar (with supplemental vitamins/minerals, polyphenolics, β-glucan, and docosahexaenoic acid (DHA)) could serve as an effective adjunct to lifestyle counseling for weight management in an inner city population.

METHODS

18 overweight, predominantly female adolescent/parent guardian dyads and 2 triads (21 adults, 22 teens, randomized as 12 intervention (INT), 8 control (C) family units, 48.7% Non-Hispanic Black, 34.1% Hispanic, and 17.0% Caucasian) were recruited from the Healthy Hearts Clinic at Children’s Hospital Oakland. Two adults dropped out. Assessment of physical (BMI, blood pressure, fitness), behavioral (diet, activity, quality of life (QOL)), metabolic (cardiovascular and diabetes risk biomarkers), and metabolomic (branched chain amino acids) status was conducted at baseline and study completion on the remaining 41 participants who attended six weekly group exercise and nutrition sessions with their cohort. Compliance with eating the supplement (INT) and home lifestyle adherence (INT and C) were evaluated with phone calls to each participating family every second day.

RESULTS

There was excellent attendance (80% of group sessions, 100% of assessment visits) in both INT and C groups. Compliance with nutrition bar intake was 85.8 ± 11.1% and 86.7 ± 13.8% among INT group adults and teens respectively. There was considerable obesity, hypertension, dyslipidemia, inflammation, and insulin resistance in all participants. Baseline diets were universally poor but improved in both INT and C groups, adults and teens, most notably decreased total fat (especially saturated fat), total carbohydrates (especially added sugars) and glycemic load. Self-report activity also trended up. Systolic BP improved in INT teens and worsened in C teens. QOL scores improved and branched chain amino acid levels fell in INT parents and homocysteine levels fell in INT parents and teens.

CONCLUSIONS

Enrollment of parent/guardians with their inner city obese teens referred for weight management resulted in excellent adherence to an intensive program of heart healthy counseling and overall improved dietary and activity habits. A nutritional supplement bar may be a valuable adjunct for metabolic health, resulting in significant reductions in blood pressure, plasma homocysteine and branched chain amino acids and improved reported QOL. It is possible that a longer term trial would result in a broader spectrum of favorable biomarker changes.
Adolescent Obesity: A Dynamic Process Analysis of American Youth

The prevalence of obesity among adolescents has increased alarmingly over the past decade. Adolescent obesity has become a major health problem for American youth due to its association with morbidities and tendency to persist into adulthood. Researchers have linked numerous social, biological and behavioral characteristics to obesity. The inability to attribute obesity to a single attribute or time suggests that obesity development and persistence is a complex process. I hypothesize that the failure of these previous studies lies in their inability to differentiate between “initial conditions” —which persistent over time—and “dynamic conditions”—which change over time. Life-course studies have provided significant evidence for a link between body weight and a range of chronic diseases. The life-course approach conceptualizes BMI development as a lifelong, dynamic process in which genetic, psychological, social and environmental factors interact to produce health states. The life-course approach is well suited to study adolescent body weight since the development of adolescent weight status is likely a multi-factor process. The two effects—persistent and dynamic—proposed in my hypothesis can be identified separately only with longitudinal, life course data. Using longitudinal data, analysis employs a dynamic modeling framework in which the adolescent's weight state is a function of observed weight state in the preceding observation period as psychological, social and environmental factors. Using a 10 year panel of youth, I employ a multivariate regression model to track BMI over time and determine the relative predictive contribution of a variety of time-related and non-time factors. I divide the data into six subgroups—white males, white females, Hispanic males, Hispanic females, black males, and black females—and analyze each group separately. After controlling for the passage of time and inherited tendencies, results show a variety of personal, lifestyle and situational characteristics contribute significantly to BMI and obesity. Many factors are contributors for all six groups, while some only play a role among few. Age, independence, urban residence, substance abuse, peer behavior, delinquency, maternal education and household size have significant impacts on the probability of overweight in most subgroups. Finally, I perform a similar analysis on underweight adolescents which shows that age, environmental and religiosity attributes contributed largely to underweight. Not only does this suggest that particular behaviors and situations can explain both underweight and obesity among American youth, but it also provides evidence that changes to particular lifestyle and behavioral characteristics can curb the growing obesity epidemic.
Insulin Pathway Component Expression and Treatment Response in Hepatitis C

The degree, if any, that insulin resistance may confound the treatment of Hepatitis C (HCV) by preventing sustained viral response (SVR) is ambiguous as numerous studies have produced contradictory results. These studies largely do not account for IL28b genotype, which is known to have a profound effect on the chance of attaining SVR.

One aim of this study is to measure the expression of genes important to the insulin signal transduction pathway in the context of SVR and IL28b genotype in Hepatitis C patients. Another aim is to establish the degree of correlation between SVR and clinico-demographic data associated with insulin resistance and metabolic syndrome.

Methods

Twelve flash-frozen blood samples from patients with HCV were obtained. Eight samples were confirmed to lack the IL28b genotype that confers a benefit to treatment response; of those, 4 patients achieved SVR after interferon and ribovirin treatment and 4 did not. The remaining four samples had the beneficial IL28b genotype, all of whom achieved SVR. RNA was extracted from the samples using a Total RNA Fatty and Fibrous Tissue Kit (Bio Rad). This RNA was then immediately converted to cDNA using the RT First Strand Kit (Qiagen). Quantitative Polymerase Chain Reaction (qPCR) was conducted for all eight samples to amplify the cDNA of the genes IRS1 and SOCS3, for which 18s was used as a reference. Clinical data was also analyzed according to Spearman’s Rank to determine the correlations among the patients.

Results

The relative transcription for SVR+ patients using the IRS1 gene was, on average, 0.00124, while the average for SVR- patients was 0.0107, making the SVR-/SVR+ ratio equal to 8.648. When using SOCS3, the average was 0.00395 for SVR+ patients and 0.00113 for SVR- patients, making that SVR-/SVR+ ratio 0.285. Therefore, relative transcription rates are increased in SVR- patients when using IRS1, and decreased in SVR- patients when using SOCS3 in comparison to SVR+ patients. The clinical data showed that obesity and glucose levels are more closely correlated with SVR+ response in patients with the CT/TT allele than in the cohort of all twelve patients.

Conclusions

There is an inverse relationship in the relative transcripts of the two genes, which suggests that in HCV patients that lack the beneficial IL28b genotype, there is differential insulin signalling between patients that achieve SVR and those that do not. After conducting this study with a larger number of samples, it may be possible to conclude that insulin resistance levels play a role in whether a patient with the less beneficial genotype will achieve SVR.
Body Mass Index (BMI) and Pesticide Exposure in a Cohort of Pesticide Applicators

BACKGROUND

Organochlorine and phenoxy herbicide pesticides have been hypothesized to play a role in obesity. Using data from a longitudinal cohort study of pesticide applicators from Iowa and North Carolina known as the Agricultural Health Study (AHS), we are testing these associations among males using BMI as the outcome variable.

METHODS

The cohort was enrolled from 1993-1997 with a follow-up 5 years later. Data are questionnaire-based with an exposure algorithm developed from responses on intensity, duration, and use of personal protective equipment (PPE). These exposure data are considered to be the best questionnaire-based exposure information available anywhere. Since our investigation required developing variables to control for diet and exercise the analysis was limited to 9,076 male applicators aged 20 years or older who completed the diet history at follow-up. Final regression models examined exposure to various pesticide classes as a continuous variable in relation to BMI. Additional potential confounders were identified: age, smoking, education, non-farm occupational exposures, alcohol use, and total years of farming. Three analyses (cross-sectional using data obtained at enrollment; prospective using exposure at enrollment and BMI at 5-year follow-up; and cross-sectional using data obtained at 5-year follow-up) have been examined.

RESULTS

We have identified increases in BMI associated with exposure to specific classes of pesticides in our regression analyses, including organochlorines and phenoxy herbicides, both of which were suggested by our literature review. Results for BMI measured at enrollment or at follow-up are consistent. Overall and stratified analyses (by state and presence/absence of relevant medical conditions) revealed consistently significant results for the association between triazine herbicides and BMI. Exposure-response analyses also supported this association.

CONCLUSIONS

We have provided enough evidence to warrant further investigation of the association between BMI and some agricultural chemicals, particularly herbicides, phenoxy herbicides, and triazine herbicides.
BACKGROUND

Yoga is a form of physical activity that has been gaining in popularity in the United States. Although the transient benefits of yoga to physical and psychological health have been demonstrated empirically, there is little information on the enduring health benefits among yogis — those practicing yoga consistently over many years.

PURPOSE

To examine differences in several dimensions of psychological well-being (general health, anxiety, depression, coping, mindfulness, and perceived stress) between yogis and those engaging in regular cardiovascular exercise and weight training.

METHODS

Participants (N = 163; male=31, female=132) were adults (18 to 65 years) recruited from yoga studios and fitness clubs in the DC Metropolitan area. Self-reported information on psychological well-being was ascertained from several validated measures via an on-line survey tool. Mean scores for the study variables were compared between yogis (n=62) and exercisers (n=101) using independent t-tests and multivariable regression modeling.

RESULTS

On average, participants were 34 years of age, primarily Caucasian (88%) and of higher educational attainment. The yoga group reported a lower prevalence of joint pain and headaches compared with the exercisers (p<0.05). Moreover, the yoga group reported higher scores for mindfulness (66.9±12 vs. 58.9±13; p<0.001), lower scores for perceived stress (12.6±5.2 vs. 14.8±5.4, p<0.05) and higher scores for coping skills (26.3±4.5 vs. 23.9±4.9, p<0.05) compared with the exercise group. Surprisingly, the two groups were similar with regard to self-reported symptoms of anxiety and depression.

CONCLUSION

The enduring and specific benefits of yoga to mindfulness and consequent stress reduction should be emphasized in community-based health promotion strategies.
Internet gambling, video game and pornography addiction: A neurobiological and psychological comparison with drug addiction and evaluation of treatment with naltrexone

**BACKGROUND. METHOD AND OBJECTIVE**

While less conspicuous than substance misuse, internet gambling, video game and pornography addiction also cause great personal harm. Moreover, these “behavioral addictions” diminish addicts’ productivity, costing employers over $50B annually. Recent studies suggest biological and psychological similarities between substance and behavioral addicts and provide nascent evidence that naltrexone, a competitive mu- and kappa-opioid receptor antagonist, may serve as a cost-effective treatment. Using recent studies of brain reward circuitry, voluntary and cued decision-making, and both types of addiction, this literature review will synthesize relevant findings in advance of possible clinical trials with naltrexone.

**RESULTS**

Middle- and upper-class whites suffering from behavioral or substance addiction (or both) tend to score highly on measures of novelty- and sensation-seeking, and addicts of either type are likely to have experienced a mood or anxiety disorder before addiction. Stress and addiction-related cues strongly drive further drug- or activity-seeking and relapse in both groups. Like substance addicts, internet addicts develop tolerance quickly, leading them to seek longer, more exotic or financially risky activities over time, and on cessation they experience similar withdrawal symptoms. Anatomical scans of drug addicts and video-game addicts reveal a striking loss of gray matter in the dorsolateral prefrontal and anterior cingulate cortices. In several observational studies of gambling addicts and one study of pornography addicts, naltrexone markedly reduced the onset and duration of addictive behaviors as well as the self-reported craving and incentive salience of reward-related stimuli.

**CONCLUSION**

From a neurobiological and psychological standpoint, behavioral addicts strongly resemble substance addicts. Naltrexone appears likely to reduce addictive activity-seeking both by lowering the incentive salience of addictive stimuli and reducing psychological stress, via blockade of mu- and kappa-opioid receptors, respectively. Full RDBPC clinical trials are needed, however, to evaluate naltrexone’s efficacy in treating internet addictions.
Bikesharing in a Community Mental Health Population in Washington D.C. as an Intervention for Improving Health and Mobility

This research project is a pilot program that would give memberships to Capital Bikeshare to interested consumers at McClendon Center, a non-profit, mental health core service agency and day treatment program in Washington, DC. Along with the membership, group classes with the Anacostia Bicycle Association on confident cycling and a helmet would be offered to prepare clients for city riding. The hypothesis is that if memberships to Capital Bikeshare are given and properly promoted to this population of mental health consumers they will be more likely to use it as a form of transportation, which would have effects on their physical and mental health as well as eliminate some of the transportation barriers that limit low-income individuals mobility. This health intervention is part of a larger trend of encouraging bicycling as a form of commuting and physical activity in low-income communities in Washington DC. Although not currently a policy discussion, this type of study may encourage DC policymakers to give reduced rates to Capital Bikeshare for mental health consumers, especially those on disability, similar to the reduced fare programs they have already established through the WMATA. This will be an opportunity for hard data documenting the positive effects of this intervention on this population. On top of the effect we expect the study to have in influencing Washington DC transportation and mental health policy, we also expect that the study will result in one major, empirical article in a peer-reviewed public health or psychiatric journal. We also expect this study to get press coverage because of our collaboration with the DC Department of Transportation who will be sending out press releases related to our partnership and the results of the study.
The association between the PACAP and NPY genes with cognitive and behavioral flexibility and stress in children with autism spectrum disorders

Restricted, repetitive, behaviors and interest (RRBI) symptoms are core to autism spectrum disorder (ASD), particularly higher-order RRBI which are related to stress cognitive and behavioral inflexibility. A limitation of previous studies is the failure to analyze the degree of high levels of stress in children with ASD. Previous research on ADI uses phenotypic information as the sole basis of analysis and thus as a result there is less power to identify gene-behavior associations in children with ASD. The PACAP gene (rs2267735) is known to predict posttraumatic stress disorder diagnosis and symptoms in females and to some degree fear. The NPY gene (rs16147) is known to explain inter-individual variations in resiliency to stress, a risk factor in many diseases. The hypothesis of this study is to see whether there is a relationship between the PACAP and NPY genes and the RRBI symptoms, which induce great levels of stress in young ASD patients. In our preliminary analyses, we have examined 45 children with ASD diagnosis. We find preliminary evidence of an association between variation at rs2267735 and rs16147 and scores on continuous measures of cognitive and behavioral dysfunctions supporting the hypothesis that the risk allele in the PACAP and NPY genes may relate to the stress levels as a result of ASD.
PSYCHIATRY/MENTAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Creating a Mental Health Educational Intervention for First Year Medical Students

BACKGROUND

A series of studies over the past decade that look into health and wellness of medical students show that cross sectional rates of depression and anxiety are higher in medical students than the general population. Medical students are also known to suffer from substance abuse disorders more than age matched counterparts. To further assess needs at GW specifically, a needs assessment was conducted by two GW medical students in 2009 which demonstrated that 15% of responders had experienced suicidal ideation. Those that experienced suicidal ideation were more likely to report depression and stress, and less likely to report that they would access help if they needed it. They also found that 36% of responders reported drinking in excess, but that reported rates of marijuana and stimulant abuse were lower than age matched counterparts. Based on this study, I created a qualitative study using focus groups to capture medical students experience with mental health problems and resources with the goal of creating an online educational program.

METHOD

I conducted a series of focus groups (2) to obtain qualitative data that characterizes the medical student experience with mental health problems. Focus groups included 12 students who had just completed their first year of medical school. I specifically looked at what resources medical students knew were available and what barriers they faced accessing these resources. Focus groups were recorded. The next step will be transcription of the focus group recordings and coding of the qualitative data into themes. Coding will enable the development of a conceptual model about medical student mental health at GW to guide the development of an online educational program.

RESULTS TO DATE

Preliminary data was obtained from listening to recordings, taking notes, and classifying data into themes. Students who participated in the focus groups were very willing to share their thoughts on their mental health while at GWSMHS. Students admitted to struggling with their adaptation to medical school. They found both adaptive and maladaptive ways to cope with their transition. They felt that GW lacked the resources they needed for their mental health. Students identified many barriers to accessing the few resources they were aware of.

CONCLUSION

Overall GW medical students do not feel that their mental health needs are being adequately met. It is unknown whether this is due to a lack of resources or a lack of visibility of resources. This program will be designed to give medical students a comprehensive understanding of how their mental health can change throughout medical school, as well as a list of resources available to them. The preliminary findings point to the need of educating incoming medical students about the mental health disorders they might face throughout school, why they are a vulnerable population, and all of the resources they have available to them when they want or need help.
PSYCHIATRY/MENTAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

The Use of Deep Breathing to Reduce Pre-Surgical Anxiety Levels

BACKGROUND

Previous studies have demonstrated that deep breathing exercises are associated with a number of physiological changes, including decreased respiratory rate, decreased peripheral sympathetic nervous system activity, and diastolic and systolic blood pressure reduction in patients with mild hypertension. Additionally, deep breathing has been shown to increase thermal pain tolerance, and increase the amplitude of vagal cardiac markers—both of which also contribute to measurable physiological changes in heart rate variability. Within the context of surgery, some researchers have also suggested that short-term surgical outcomes may improve with pre-operative stress management.

METHODS

Fifty-one ambulatory surgery patients were included in this study. Patients were chosen based on availability at the time of check-in, and randomly assigned to one of three experimental groups: a control group, a deep breathing group, and a cognitive behavioral therapy group.

Approximately 24 hours before their scheduled surgeries, patients were informed of the study objectives, offered the option to consent or withdraw, and taught a simple deep breathing or cognitive behavioral therapy, when appropriate. Before learning either technique, patients completed a State-Trait Anxiety Inventory (STAI), rating their level of anxiety. Patients were then asked to practice their learned technique twice before their surgery, and again once after surgery. Twenty four to forty eight hours after their surgery, a second STAI was administered and the two scores were compared.

RESULTS

When compared to the current standard of care, patients experienced a minor decrease in anxiety levels when using the deep breathing technique and a moderate decrease in anxiety, with the use of cognitive behavioral therapy. These changes were denoted by a 0.88 point increase (p =0.29) in STAI inventory scores for the control group, and 3.25 (p= 0.40) and 1 STAI point (p = 0.33) decreases for cognitive behavioral therapy and deep breathing groups, respectively.

CONCLUSIONS

The results of this study suggest that some therapeutic interventions may contribute to a decrease in pre-surgical anxiety levels. Although the deep breathing technique appeared to be less effective than cognitive behavioral therapy in the management of pre-surgical anxiety, it should be noted that the level of pain that some patients were experiencing during recovery may have inflated post-surgical anxiety scores. Also, mid-way through the study, it was discovered that some patients were receiving anti-anxiety medications on the morning of their surgery. This was a significant confounding variable, which was out of the control of the researcher.
Access to Psychiatric Care Among Patients with Depression Presenting to the Emergency Department

BACKGROUND

Literature suggests that there is a high rate of Major Depressive Disorder (MDD) in emergency department (ED) users. However, access to outpatient mental health services is often limited due to lack of providers. As a result, many persons with MDD who are not in active treatment may be more likely to utilize the ED as compared to those who are currently undergoing outpatient treatment.

OBJECTIVES

Our study evaluated utilization rates and demographic characteristics associated with patients with a prior diagnosis of MDD not in active treatment. We hypothesized that patients who present to the ED with untreated MDD will have more frequent ED visits.

METHODS

This was a single center, prospective, cross-sectional study. We used a convenience sample of non-critically ill, English speaking adult patients presenting with non-psychiatric complaints to an urban academic ED over 6 months in 2011. Subjects were surveyed about their demographic and other health and health care characteristics and were screened with the PHQ 9, a 9 item questionnaire that is a validated, reliable predictor of MDD. We conducted bivariate (chi squared) and multivariate analysis controlling for demographic characteristics using STATA v. 10.0. Our principal dependent variable of interest was a positive depression screen (PHQ 9 ≥ 10). Our analysis focused on the subset of patients with a prior diagnosis of MDD with a positive screen for MDD during their ED visit.

RESULTS

Our response rate was 90.7% with a final sample size of 1012. 243 (24.0%) patients screened positive for MDD with a PHQ 9 ≥ 10. Of the 243 patients with a positive depression screen, 55.1% reported a prior history of treatment for MDD (n=134). Of these patients, only 57.6% were currently actively receiving treatment. Hispanics who screened positive for depression with a history of MDD were less likely to actively be undergoing treatment as compared to non-Hispanics (22.2% versus 46.9%, p=0.041). Patients with incomes less than $20,000 were more likely to actively be receiving treatment as opposed to higher incomes (76.3% versus 42.7%, p=0.003).

CONCLUSION

Patients presenting to our ED with untreated MDD are more likely to be Hispanic and less likely to be low income. The emergency department may offer opportunities to provide antidepressant treatment for patients who screen positive for depression but who are not currently receiving treatment.
Reconceptualizing the Bender Visual-Motor Gestalt Test: Toward New Applications

In educational, medical, rehabilitation and mental health settings, brief, accurate diagnostic screening tools are essential to ensure access to necessary services. As healthcare and other service systems grapple with increasing demand and decreasing budgets, the necessity of differentiating emotionally based psychiatric disorders (such as depressive and anxiety disorders) from cognitive, affective, learning, perceptual, and behavioral abnormalities stemming from neuropsychological deficits is crucial. Misdiagnosis leads to wasted funds and misguided and ineffective interventions. While a substantial body of literature has established the utility of assessing visual-motor integration as perhaps the most effective means of screening for neuropsychological impairment, multiple assessment measures continue to vie for professional attention, disturbingly often without adequate conceptual basis or empirical validation.

In contrast, almost 75 years of clinical experience have established the Bender Visual-Motor Gestalt Test (Bender) as a valid, reliable, inexpensive, fast, and culturally-sensitive neuropsychological screening measure. However, challenges have arisen as research into the measure has lagged, debates about scoring systems have remained unresolved, and clinical usage patterns have shifted. This has made it difficult to reach consensus on how to use visual-motor gestalt tests, especially the Bender, in modern clinical psychology practice. There is no extant contemporary review of the Bender literature, surprising in light of the introduction of updated, psychometrically robust versions of the test (Brannigan & Decker, 2006; Reynolds, 2007). Nor is there an updated conceptual basis for use of the Bender, aligned with contemporary thinking in neuropsychology, neuroimaging, and neuroscience.

Our research team presents a re-conceptualization of the role and potential applications of the Bender, and a proposal for pilot research at GW to define exciting potential uses for this measure.
Children with Chronic Myositis Understate Physical Capabilities while Overstating Self-Advocacy

BACKGROUND
The American Academy of Pediatrics recently highlighted the importance of addressing transition of care tasks for children with chronic disease by publishing a policy statement in July, 2011 (1). The AAP highlights the importance of addressing barriers to the active participation of children in the management of their own medical problems. To this end, we conducted a study to assess knowledge, self-advocacy, and readiness for myositis patients to transition from pediatric to adult care.

METHODS
We employed “survey monkey,” an online website for the anonymous collection of data in order to compare the experiences of children and their parents, separately and individually, with regard to issues relating to transition readiness. Patients and their families were solicited from the US and Canada through established clinics for children with idiopathic inflammatory muscle diseases, as well as with the aid of a nonprofit organization for the benefit of such individuals (http://www.curejm.com/). The unique ability to compare, in aggregate, parents’ and patients’ answers enabled us to uncover deficiencies as well as discrepancies revealed by patient and parent reporting.

RESULTS TO DATE
We analyzed the responses of children, aged 15 years or less, along with their parents’ (Table 1). 221 different parents’ responses were compared with the responses from 54 children. Not unexpectedly, children tended to attribute greater competency in self-advocacy and self-knowledge as compared to their parents.

Table 1. Parents vs. Patients 15.0 years of age and younger

<table>
<thead>
<tr>
<th>Survey Item</th>
<th>Parents(n=221)</th>
<th>Patients(n=54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does your child know where to get her/his doctor’s phone number?</td>
<td>64 (31.2%)</td>
<td>35 (52.1%)</td>
<td>0.0111</td>
</tr>
<tr>
<td>Right now, can your child climb the stairs without help or using support?</td>
<td>177 (83.1%)</td>
<td>37 (68.5%)</td>
<td>0.0218</td>
</tr>
<tr>
<td>Right now, can your child stand from a seated position without assistance or support?</td>
<td>190 (93.1%)</td>
<td>49 (90.7%)</td>
<td>0.8095</td>
</tr>
</tbody>
</table>

For example, children overstate their ability to make their own doctor’s appointments. In contrast, children understate their self-assessment of physical capabilities. Specifically, parents were statistically more likely to assert that their children were able to climb stairs without help or support ($p < .03$).

DISCUSSION & CONCLUSION
Our results are particularly striking because physical development is objective. While patients and their parents agree on the ability to arise from a seated position, they do not agree on stair climbing capability. Therefore, either, 1) patients with myositis may evidence regressive behavior or, 2) parents may be experiencing anxiety concerning their children’s limitations. Further study on the psychosocial interaction between parents and children with myositis should emphasize the child’s involvement in playing the “sick role” either as a reaction to stress or a way to seek positive encouragement from their parents and peers. In addition, research should address the possibility of parents overestimating their child’s physical functioning owing to an unconscious desire to push unacceptable emotions aside.

REFERENCES
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PSYCHIATRY/MENTAL HEALTH

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Do Neighborhood Characteristics Prompt Earlier Cannabis Use in Patients Diagnosed with First-Episode Psychosis

Accumulating evidence suggests a complex link between psychotic disorders and cannabis misuse (Ramsay & Compton, 2011). In fact, premorbid cannabis use may be associated with an earlier age at onset of prodromal and psychotic symptoms. Given that cannabis use is a complex behavior driven by genetic, social, and environmental influences, the role of neighborhood is worth considering. Recent research indicates that neighborhood impacts various health conditions, ranging from obesity in older adults (Glass et al., 2006) to intimate partner violence (Li et al., 2010).

OBJECTIVE

We hypothesized that neighborhood socioeconomic and stability characteristics would contribute to ages at onset of premorbid cannabis use in first-episode patients.

METHOD

We combined data from 2 consecutive first-episode samples (n=200) gathered in Atlanta, Georgia. Into this dataset, we imported U.S. Census Bureau census tract-level data and performed exploratory factor analysis on 17 census tract variables, which revealed 3 distinct neighborhood factors that describe local attributes of the first-episode patients’ environmental surroundings. Specifically, the 3 factors were labeled disadvantaged neighborhood (e.g., percentage of families living below the poverty level), immigrant neighborhood (e.g., percentage foreign-born), and transitory neighborhood (e.g., percentage of renter-occupied units). Continuous scores on these three factors were trichotomized to generate tertiles that indicated high, medium, and low levels of socioeconomic disadvantage, immigrant population, and transitory population. Also taking into account the effects of gender, we examined 3 dependent variables: age at first use of cannabis (n=143), age at beginning weekly use (n=106), and age at initiation of daily use (n=83). Using 2-way analyses of variance, we examined the role of the 3 neighborhood factors and gender (given its known relation to cannabis use initiation and escalation; Brook et al., 1999) in predicting these age-of-use variables.

RESULTS

Neither the extent of socioeconomic disadvantage nor transitory factor scores were predictive of age at initiation, weekly, or daily cannabis use. However, there were significant associations between the immigrant factor score and age at initiation (p=0.041), weekly (p=0.048), and daily (p=0.004) use of cannabis. Throughout, gender remained significant for age at onset of weekly and daily use of cannabis, though gender was not a significant predictor of age at initiation of cannabis use.

CONCLUSION

Our hypothesis that neighborhood characteristics prompt earlier use of cannabis in first-episode psychosis was partially supported in terms of the significant relationship between age at initiation and age at onset of weekly and daily cannabis use and the aforementioned immigration score, though results may be limited by the relative homogeneity of the study sample. Gender appears to play a larger role in escalation of cannabis use.
Understanding Adherence Barriers to Antidepressants among an Urban Latino Population: Insights from providers and patients about risk factors, protective factors and interventions

BACKGROUND
Lack of adherence to antidepressant medication has been well documented as a major difficulty in the successful treatment of Major Depressive Disorder, especially among the US Latino population. The objectives of the study were to identify the primary causes of decreased adherence to antidepressant medications among the urban Hispanic population in Seattle, WA, as well as evaluate resource and intervention strategies to address those barriers.

METHODS
The inquiry was done in two phases. In the first phase, online journal articles meeting search criteria were reviewed and compiled to generate a list of identified barriers to the adherence to antidepressant treatment strategies. In the second phase, interviews were conducted with patients, family practice physicians, mental health specialists, and patient advocates for Latino patients to confirm identified barriers as well as evaluate the usefulness of intervention strategies to improve adherence.

RESULTS
Risk factors were compared between literature reviews and interviews, identifying a list of factors perpetuating non-adherence among the US Latino population. These include: stigma towards medication, poor therapeutic alliance, limited financial and familial support, lower socioeconomic status, access barriers to care, fear of dependence and side effects, lack of familiarity with US medical care delivery, preference for natural remedy, and others. Protective factors identified include: family support, acculturated providers, understanding of mental illness, positive therapist relationships, and follow up. Successful Interventions identified include: group therapy, PCP management of depression, SW/therapist partner, and concrete advice given.

CONCLUSIONS
Among the expert opinion gathered and review of the literature a number of themes were found repeated which are crucial to understanding the difficulties patients have with adhering to antidepressant treatment regimens. The dominant three themes were found to be: patient’s fear of medication dependence, patient’s lack of knowledge about depression as an illness and unfamiliarity with treatment, and patient’s individual and cultural identity. In the analysis of patient feedback and with the insight of medical professionals in the field, important themes regarding intervention strategies surfaced, pointing to the importance of a relationship focus, behavior-focused therapy, and culturally-knowledgeable providers.
SCHOOL OF MEDICINE AND HEALTH SCIENCES

Modulation of μ-Opioid Receptor Mediated Analgesia, Tolerance and Hyperalgesia in Children and Adolescents

BACKGROUND

Opioids typically provide sufficient perioperative analgesia, however some pediatric patients require escalating dosages for proper pain management despite increasing side effects. This tolerance and/or hyperalgesia poses a significant problem, especially with the high-dose intraoperative and long-term postoperative opioid requirements of exceedingly painful surgeries. Such effects are attributed to μ-receptor agonist activation of NMDA receptors and are therefore subject to inhibition by ketamine, an NMDA receptor antagonist. Opioid-induced miosis is the most sensitive indicator of opioid efficacy due to its resistance to the development of tolerance. Consequently, pupillometry can identify the onset of tolerance or hyperalgesia, a decreased miotic response or a mydriatic response, respectively, versus non-tolerant patients with dose-response increases in miosis. This study will establish ketamine’s role in blocking the development of tolerance and/or hyperalgesia, thereby decreasing opioid requirements and adverse side effects, and assess pupillometry as a noninvasive means of identifying the onset of these phenomena.

METHODS

Ninety children 10 to 18 years old undergoing posterior spinal fusion with instrumentation were randomized to either the ketamine-treated group or the placebo-controlled group. Preoperatively, baseline static and dynamic pupillometric data was recorded. The ketamine group received a 0.5mg/kg IV load followed intraoperatively by a continuous infusion at 0.25mg/kg/h and postoperatively at 0.1mg/kg/h for a total duration of 72 hours. The placebo group received saline at the same rates and duration. Intraoperative remifentanil administration was recorded along with postoperative morphine requirements. Daily and cumulative morphine consumption was correlated with pupillometric data and side effects through postoperative days 1-4.

RESULTS

This study is incomplete and remains blinded; therefore, final results and analyses are currently unavailable. However, preliminary data from the two blinded groups, A and B, revealed a mean cumulative morphine consumption (mg/Kg bodyweight) of 3.8mg/Kg in Group A and 4.7mg/Kg in Group B. Additionally, the mean change in maximum pupil diameter was 0.11mm and 0.62mm for Groups A and B, respectively.

CONCLUSIONS

Despite current limitations, the two treatment groups demonstrated distinct differences in both cumulative morphine requirements and changes in maximum pupil diameter postoperatively. Group A showed a 0.9mg/Kg decreased morphine requirement and 0.51mm less pupil redilation compared to Group B. Group A results illustrate the opioid-sparing effect and dose-dependent miosis expected from ketamine-induced inhibition of tolerance and/or hyperalgesia. These conclusions are based off of current, preliminary data. Further analyses and conclusions will be drawn upon completion of the study.
REHABILITATION AND RECOVERY

MEDICAL FACULTY ASSOCIATES

Retrospective Prevalence of Myofascial Tender and Trigger Points in Patients Presenting with Cervico-Thoracic and Lumbro-Sacral Spine Related Pain

To retrospectively report the prevalence of tender points and trigger points at The George Washington University (GW) Spine & Pain Center in patients presenting with cervico-thoracic and lumbro-sacral spine pain, differentiating each based on referral patterns. To organize the data according to specific diagnoses and correlate the specific innervations of the associated tender point and trigger point muscles.

DESIGN
Retrospective.

SETTING
Tertiary Spine & Pain Center.

PARTICIPANTS
11 subjects with cervico-thoracic spine related pain and 13 subjects with lumbro-sacral spine related pain.

INTERVENTIONS
We tested for the presence/absence of cervical/lumbar tender and/or trigger points and the minimum pain pressure threshold reading of those points using a digital algometer.

MAIN OUTCOME MEASURES
Presence or absence of tender and trigger points, minimum pain pressure threshold.

RESULTS
82% of patients with cervical spine related pain were found to have tender/trigger points in specific muscles. Patients with lesions in C3-C4 presented more commonly with both tender and trigger points located in the middle trapezius; C5-C6 lesions with tender points in biceps brachii, brachioradialis, pectoralis major; C5-C6 lesions with trigger points in pectoralis major; and C6-C7 lesions with tender points in latissimus dorsi and triceps brachii. 62% of patients with lumbar spine related pain were found to have tender/trigger points in specific muscles. Patients with lesions in L2-L3 and L3-L4 presented more commonly with both tender and trigger points located in adductor longus; and L5-S1 lesions with both tender and trigger points in tibialis anterior, soleus, and biceps femoris. The majority of diagnoses made in these patients with cervical and lumbar spine pain included spondylitis, disc bulging, and spinal stenosis. No adverse effects noted from pressure algometer usage.

CONCLUSIONS
Tender and trigger points appear more likely to occur in specific muscles in the presence of spinal pathology.

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Clinical Decision Making in the Acute Care Environment: A Survey of Practicing Physical Therapists

BACKGROUND
A variety of formal guidelines are available to assist physical therapists in determining when exercise testing would be contraindicated or when a graded exercise test should be terminated. Guidelines to address absolute or relative contraindications for participating in activities of daily living (ADL) or therapeutic exercise as part of a physical therapy plan of care are often inferred or non existent. Therefore the purpose of this study was to investigate current physical therapy practice trends in the acute care environment using a case-based clinical decision-making survey, in order to clarify when exercise or ADL training would be contraindicated.

METHODS
Physical therapists from the acute care and cardiovascular and pulmonary American Physical Therapy Association (APTA) section membership participated in an 8-question clinical decision-making survey. Choices included decisions “to treat” or “not to treat” based on medical information provided. Cases ranged from treating a patient post hip replacement with a diagnosis of deep venous thrombosis, to treating a patient post Q wave MI who presented with pedal edema, jugular venous distention (JVD) and crackles. Additional comments regarding practice choices were solicited and analyzed. Demographic information was also collected.

RESULTS
356 PTs responded to the survey (18% response rate). Number of correct responses was calculated per case. Responses were also analyzed by educational training and years of clinical experience. Respondents chose the optimal treatment choice more than 80% of the time in five of eight cases. Mean scores ranged from 4.85/8.0 for bachelors-trained physical therapists with less experience, to 6.76/8.0 for doctorally-trained physical therapists with greater experience. A two-way ANOVA indicated a significant main effect for educational training and years of experience and also a significant interaction (p=.017). Incorrect responses in one of the eight cases appeared to be related to therapists using outdated information regarding mobilization following administration of LovenoxTM or institutional guidelines.

CONCLUSIONS
Physical therapist who are acute care and cardiovascular and pulmonary section members appear to be utilizing current evidence to support their clinical decision making process in the acute care environment. Physical therapists with more experience, and those who continued their professional education were more likely to choose the optimal treatment strategy.
Eccentric Training for the Rehabilitation of a High Level Wrestler with Distal Biceps Tendinosis: A Case Report

BACKGROUND AND PURPOSE
Distal biceps brachii tendinosis is a relatively uncommon clinical diagnosis seen in physical therapy. As a result, there is little evidence guiding clinical decisions regarding best practice or effective conservative treatment options to restore individuals to their previous level of function. Specifically, the physical rehabilitation of distal biceps tendinosis has yet to be described in detail in available literature. Eccentric training has been shown to be beneficial in the rehabilitation of upper and lower quarter tendinoses, leading to decreased pain and increased function. The purpose of this case report is to describe the development and demonstrate the use of eccentric training for the rehabilitation of distal biceps tendinosis.

CASE DESCRIPTION
A 41-year-old male presented to a university outpatient physical therapy clinic with a two month duration of pain in the right antecubital space which occurred when the patient was performing close-grip resisted curl ups for the first time. Sharp pain was noted in the right arm during the lowering phase. Following clinical examination including diagnostic ultrasound, distal biceps tendinosis appeared to be the likely diagnosis. The patient was educated and trained with eccentric loading for right elbow flexion with the forearm in neutral and in supination.

OUTCOMES
The patient was seen in physical therapy for three visits over the course of four weeks. Following eccentric training, the patient reported decreased pain, demonstrated increased right elbow flexion and forearm supination strength, was no longer tender to palpation of the distal biceps tendon and showed clinically significant improvement in QuickDASH scores.

DISCUSSION
After performing a comprehensive differential diagnosis and determining a patient to have distal biceps tendinosis, conservative measures should be trialed in order to optimize the patient’s current level of function. Given the lack of available research on the rehabilitation of distal biceps tendinosis, eccentric training showing benefits with other upper quarter tendinoses and the positive outcomes in this case, it may be appropriate for physical therapists to employ eccentric training for patients with distal biceps tendinosis.”
Anesthetic Management of a Parturient with Chronic Lyme Disease: A Case Report and Review of Literature

BACKGROUND

Lyme disease, caused by the spirochete Borrelia burgdorferi, is the most common vector-borne disease, affecting approximately 20,000 people in the United States per annum1. Its symptoms can include fever, headache, fatigue and the skin rash erythema migrans. If untreated, it can progress to arthritis and, rarely, can lead to neurologic sequelae such as cranial nerve palsy, polyneuropathy, encephalitis, encephalopathy, and meningitis. A minority of patients will develop relapsing symptoms of chronic Lyme disease, caused by persistent infection with B. burgdorferi despite an adequate course of antibiotic therapy2. Although the potential adverse effects of Lyme disease during pregnancy have been previously described3,4, there are no known published case report on the anesthetic management—specifically the effects of neuraxial blocks—of parturients with chronic Lyme disease.

CASE DESCRIPTION

The patient is a 34-year old G1P0 parturient who presents at 39.3 weeks gestation age for primary Cesarean section due to breech fetal presentation. The pregnancy is otherwise uncomplicated. The patient reports a history of chronic Lyme disease diagnosed four years prior through IgM Western blot. Her symptoms include persistent vertigo, paresthesias, headaches, low grade fever, and fatigue. MRI examination reveals enhancement in the 7th and 8th cranial nerves. After explaining the risks, including the potential worsening of her neurologic symptoms, informed consent for neuraxial block was obtained. An epidural catheter is placed atraumatically using a 17-gauge Tuohy needle in the L4-L5 interspace. Bupivacaine 0.5% 20 ml is administered slowly in the epidural catheter until an adequate level of surgical anesthesia is achieved. Her intraoperative course is unremarkable. She received a patient controlled epidural anesthesia infusion of bupivacaine 0.0325% with fentanyl for post-operative pain control (continuous 15 ml, bolus 3 ml, lockout 10 minutes). The epidural block regressed after 3 hours with return of baseline neurologic function. The catheter was discontinued 24 hours after delivery.

DISCUSSION

Although maternal-fetal transmission of Lyme disease was first described in 19856, its exact incidence in the pregnant patient is unknown, and the anesthetic management of these parturients who present during delivery is unclear. Nonetheless, neuraxial block has been successfully used in other infectious diseases causing inflammatory polyneuropathies, such as Guillain-Barre syndrome and chronic inflammatory demyelinating polyneuropathy. In this patient, we elected to perform an epidural, as opposed to spinal anesthesia, which can exacerbate certain pathologies involving the central nervous system. This case describes the first safe administration of epidural anesthesia in a parturient with chronic Lyme disease.
What Information is Available on the Internet about Safe Infant Sleep Recommendations? Let’s Google It

OBJECTIVES
Google is frequently used to access medical information. We used Google searches to determine the accuracy of information on infant sleep safety available on the internet, when compared to AAP recommendations. We hypothesized that most websites found through our searches would accurately reflect AAP recommendations.

METHODS
We searched for advice using 13 key phrases relating to infant sleep safety. Websites were categorized by type and assessed for accuracy, based on AAP recommendations. Website information was classified as “accurate,” “inaccurate,” or “not relevant.” The first 100 websites for each key phrase were analyzed.

RESULTS
Overall, 43.5% of the 1300 websites provided accurate information, 28.1% provided inaccurate information, and 28.4% were not relevant. “Infant cigarette smoking” (82%), “infant sleep position” (74%), and “infant sleep surface” (73%) resulted in the highest percentage of websites with accurate information. “Pacifier infant” (14%), “infant home monitors” (18%) and “infant co-sleeping” (20%) resulted in the lowest percentage of websites with accurate information. Government websites (80.9%) and blogs (30.9%) had the highest and lowest rates of accuracy, respectively.

CONCLUSION
The internet frequently contains inaccurate information about infant sleep safety. Providers should realize the extent to which parents rely on the internet for information about infant sleep safety.
BACKGROUND

Female Community Sex Workers (FCSWs) in India represent a vulnerable segment of the population due to the nature of their work. Young women in this line of work lack basic knowledge on their reproductive health as they progress through different stages of their life, particularly in relation to the menstruation cycle, menopause and breast cancer.

Improving women's health in India includes addressing cultural barriers such as gaps in mother-to-daughter knowledge transfer of information on menstruation and general sexual education. Institutionally, sexual education is not taught in most schools. A 2009 Indian Parliament condemned sexual education and several states banned it citing the potential for a rise in promiscuity.

A lack of knowledge about menopause and its management causes many aging Indian women to be fearful about their sex life and their attractiveness. This is particularly of concern for FCSWs who are dependent on their line of work to survive.

Breast cancer is on path to become the most common cancer in Indian women by 2020. Incidence rates increase yearly due to a variety of factors including: the westernization of Indian culture, high stress at younger ages, a rise in pollution, later marriage, fewer children and later breastfeeding. Breast cancer mortality rates have more than doubled in the last 20 years and a majority (70%) of cases aren't recognized until Stage 3. Only 3% of Indian women have regular mammograms, making breast care including self-exams crucial to their health.2,3

Aastha Paarivar (AP), is a body of community organizations, formed to address HIV/AIDS and health related community needs among female sex workers in Mumbai and Thane. The purpose of this project was to develop a culturally appropriate health curriculum and training materials for peer-led health trainings among sex workers.

METHODS

The Aastha Parivaar student team began with a literature review of health indicators in India with a focus on women's health. This review also explored existing educational materials currently used by organizations working with sex workers. The team established contact with AP to determine the type of training materials their organization desired to help facilitate their educational efforts. Their request for training materials on menstruation, breast cancer, and menopause ultimately led to the division of our team into three separate groups corresponding with each topic. Each group researched existing training materials available for women in the United States and then tailored the materials for the target population.
RESULTS
The Aastha Parivaar student team developed a culturally appropriate reproductive health curriculum and training materials for peer health training among FCSWs. The materials were designed in response to a request from AP officials who had determined there was a need for a more comprehensive and formal educational package for this audience. Based on this request and more detailed conversations regarding the materials desired, a proposed educational kit was designed for AP. The materials include a visual aid to support each training module, and peer-led health educator scripts to be used during educational sessions.

Given the vast amount of information that could be discussed with female sex workers regarding their reproductive health, we narrowed the scope to include three sections: menstruation, breast cancer, and menopause. Our final product is a comprehensive set of training materials to aid female community sex workers in Mumbai and Thane to understand their reproductive health systems, enabling them to lead healthier lives.

CONCLUSIONS
The peer, or lay health worker model has been widely used across a number of health topics to make significant improvements in health. Application of this model to community sex workers with little to no exposure to health education should serve as an appropriate introduction to a peer-led curriculum addressing key subject areas such as reproductive health in a culturally relevant manner. As this curriculum is implemented, facilitators may be able to adapt the teaching module and expand it to include additional female audiences or new health topics.
Can Written Information Improve Factual Recall and Satisfaction Following the Prenatal Consult? A Randomized Controlled Trial

BACKGROUND
How best to guide families through the decision-making process at the limits of viability remains unknown.

OBJECTIVE
To determine whether the provision of written information about prematurity can improve factual recall and satisfaction following the prenatal consult.

METHODS
We conducted a randomized controlled trial of expectant mothers from 22 to 30 weeks GA. Eligible women received routine prenatal consultation prior to enrollment and randomization. Women in the control group received written information about breast feeding. Women in the intervention group received the same breast feeding information as well as additional written information about prematurity. A survey was then administered to elicit their factual recall and satisfaction.

RESULTS
Thirty-two women completed the survey. This sample size was calculated to detect a difference of 15 points with 80% power. There was no significant difference in mean factual recall score between the groups (control 76%; intervention 71%). There was also no significant difference in mean satisfaction score between the groups (control 4.31; intervention 4.18).

CONCLUSIONS
In this study, providing written information about prematurity to expectant mothers did not improve their factual recall or satisfaction. This finding suggests that written information is not an effective way to deliver information to women in preterm labor. The poor performance of many participants on the test of factual recall indicates that they may not be adequately informed by this process, despite their high level of satisfaction.
CHILDREN’S NATIONAL MEDICAL CENTER

Improving Communication between the Emergency Department and Primary Care Physicians through Electronic Mail

INTRODUCTION
Electronic communication is an increasingly used form of communication in almost every work setting, especially the health care field. However, health care providers are slower to warm up to electronic communication compared to other fields. As a result, electronic communication has not yet been thoroughly proven to be an efficient way of communication. Information regarding the most efficient and preferred mode of communication between clinicians remains poorly understood.

OBJECTIVE
To record the prevalence of electronic communication and health related use by community physicians whose patients were admitted into the pediatric Emergency Department. Our aim is to assess level of interest among community pediatricians in communicating with the ED about their patients through electronic mail (email), instead of current communication by non-email methods (e.g. phone/fax).

METHODS
A prospective study of community pediatricians identified from a physician database for the greater Washington DC metropolitan area was conducted. Participants were randomly selected to receive communication either by email method or non-email method. Each participant was asked about their interest in communicating with the ED by email. Secondary outcomes assessed interest in electronic communication, based on survey responses.

RESULTS
A total of 1289 physicians were eligible for study inclusion. Of these, 955 (74%) were successfully contacted to participate in the questionnaire. Of the 955, 340 were selected to be in the non-email group and 655 were in the email group. In the non-email group 331/340 (97%) were successfully contacted, compared to the email group in which 432/655 (65%) were successfully contacted. The survey response rate was higher (124/340 [36%]) in the non-email group compared to the email group (68/655 [10%]). Overall interest in email communication with the ED for all participants was 114/192 (59%), and among these respondents, a higher proportion (84/124 [68%]) from the non-email group preferred email communication with the ED, compared to the email group (30/68 [44%]).

CONCLUSION
Although our email survey response rates from the community pediatricians was low compared to the non-email group, there is still a large general interest in email communication, suggesting that email communication may be a viable alternative to current method of communication by phone and fax. This could be a necessary step towards establishing an electronic communication network that would enhance access to patient medical records by involved physicians, and improve patient health care.
Factors Influencing Adolescent Females’ Choice of Hormonal Contraception

Communication is an integral component of the doctor-patient relationship necessary for effective patient care, especially in the realm of providing reproductive health services for adolescents. The use of hormonal contraceptives among sexually active adolescent females is widespread, but trends in the formulations of choice are changing. Since gaining popularity in the mid-nineties, injectable contraceptives such as Depo-Provera (DP) have increased to 21% of all hormonal contraceptives used by females aged 15 to 19 (CDC 2010). It is beneficial for physicians providing care to adolescent females to understand the factors that influence their selection of a particular type of birth control. This awareness may provide insight into where patients obtain information to help providers better understand the patient’s perspective and to foster effective avenues of communication with the patient. Through twenty-eight patient interviews conducted at the Adolescent Health Center of Children’s National Medical Center, this pilot study aimed to explore the influence of mothers/female guardians and friends on adolescent females’ selection of DP as their contraception of choice. We suspected that the female adolescent patient’s decision to initiate DP for contraception was equally influenced by communication with their mother/female guardian as by communication with their friends. The survey explored patient satisfaction with DP, the sources of information patients utilized to inform their choice of contraception, and the communication dynamics between the patients and their mother/female guardian and friends. The results of the pilot study suggest that our patient population’s decision to initiate DP as a form of contraception is more influenced by their mother/female guardian than by their friends. Further studies of larger sample size with more comprehensive exploration of the elements of communication that differ between patients and their mothers/female guardians and friends are warranted to determine why adolescent females consult with each group. With increasing awareness of these factors, providers can develop new communication strategies targeted towards sources that adolescent females trust.

SCHOOL OF MEDICINE AND HEALTH SCIENCES

Incidence of Bacterial Vaginosis in Underserved Women in Cusco, Peru

INTRO
Bacterial Vaginosis, BV, is a vaginal infection associated with poor pregnancy outcomes as well as other sexually transmitted infections. The purpose of this study was to determine the number of women who presented with bacterial vaginosis to a clinic in rural Peru and to determine significant contributing or predisposing factors.

METHODS
This retrospective chart review included all women who visited the obstetrical nurse at the Policlinico de Belen in Cusco, Peru between March 2010 and March 2011. Patients presenting to the nurse for care were screened for BV using Amsel Criteria. Clinical information including age, parity and other demographic variables were recorded at this visit. Multivariate analyses were conducted to examine the association between BV diagnosis and these demographic variables.

RESULTS
We included 1,176 unique visits and determined that 35.7% of the women were diagnosed with bacterial vaginosis. Of the 35.7% that were diagnosed with BV 73% met three out of four Amsel Criteria. Selected demographic variables were included in multivariate models and it was not significantly predict BV status.

CONCLUSION
The percentage of women diagnosed with BV is similar to the percentage of Latina women diagnosed with BV in the United States according to the 2007 article “The prevalence of bacterial vaginosis in the United States, 2001-2004; associations with symptoms, sexual behaviors, and reproductive health” published in Sexual Transmitted Diseases. In addition there is a need for stricter diagnosis criteria at the Policlinico de Belen considering over 25% of the women diagnosed with BV did not meet three out of four Amsel Criteria and therefore did not require the treatment they received.
The debate over routinely recommending dehydroepiandrosterone (DHEA) supplementation as complementary therapy for women with diminished ovarian reserve undergoing IVF – A synopsis and updated review

OBJECTIVE
The primary objective was to perform a literature review on the use of dehydroepiandrosterone (DHEA) supplementation as a complementary therapy for women with diminished ovarian reserve (DOR). The secondary objectives include an attempt to summarize the pros and cons of using DHEA in the infertile patients population and to help facilitate informed decisions regarding its integration into fertility treatment protocol.

METHODS
I performed an online search using PubMed, Medline, EMBASE, and the Cochrane databases using the following key words: dehydroepiandrosterone, DHEA, infertility, ovarian reserve, diminished ovarian reserve, DOR, poor responders, advanced maternal age, ovarian aging, ovarian function, ovarian stimulation, controlled ovarian stimulation, COH, in vitro fertilization, and IVF. Manual searches of reference lists were also performed in order to identify additional relevant literature.

RESULTS
The best evidence available, which includes results from only one prospective RCT, suggests that DHEA supplementation may improve IVF outcomes, chances of pregnancy, and the probability of live birth in women with DOR. Reasonable doubt is elicited in the literature on account of the deficient quantity and quality of the studies to date. In light of the evidence and associated skepticism, a debate has arisen over whether physicians should or not to recommend DHEA supplementation to their DOR patients. Proponents argue that given the evidence and minimal published side-effects, patients should be given the choice. Opponents rebut that given unsatisfactory evidence and the side-effects, however minimal, patients should be protected from undesirable consequences that may occur if a potentially costly therapy of unproven efficacy is recommended clinically.

CONCLUSIONS
In the field of REI, there is significant disagreement in the literature with regard to the clinical recommendation of DHEA supplementation for women with DOR. The opposition argues that the recommendation has outpaced the evidence supporting its integration into common practice. The gap between utilization and evidence must be addressed and a larger body rigorously designed, prospective randomized studies are needed to ascertain detailed patient indications and determine best practice guidelines. Several recent US trends signify the relevance and importance of this topic in medicine and public health. These include: the increasing population of women of advanced maternal age, the increasing use of infertility services (especially IVF), and the increasing use of over-the-counter dietary supplements.
Obstetric fistula is an injury that results from prolonged, obstructed childbirth leading to a hole between the vagina and bladder and/or rectum. It affects at least 441,000 women in Kenya alone, and 2 million worldwide, with up to one hundred thousand new cases developing per year. Obstetric fistula can be prevented by routine medical care such as contraceptive access and skilled birth attendants; as such, it affects the most powerless members of society and reflects a deep-seated crisis of gender equality and reproductive justice. The physical disabilities, pain, and propensity for infection in obstetric fistula patients is compounded by the shame and humiliation that is imposed upon these women by their families, their communities, and sometimes even their health care providers. While this may paint a bleak picture, the story of fistula is actually one of great hope: the average cost of a surgical repair is $300, a procedure that is successful in greater than 90% of cases. Contraception is even less costly. The multifaceted nature of this health crisis requires a dynamic approach. Not only do we need skilled surgeons, but also a comprehensive strategy that addresses the emotional and psychosocial issues afflicting these women, as well as the underlying discrepancies that factor into fistula development. While at Kenyatta National Hospital in Nairobi, Kenya, I examined both the objective and subjective story of women presenting to the "2011 Obstetric Fistula Camp." First, I coordinated a research project as a part of a larger international study looking at the socioeconomic and health factors of women presenting with obstetric fistula. In addition to this more classical research, I explored the intersection of storytelling and human expression as a means of healing. During their 1-2 week hospital stays, often sleeping two to a bed, I encouraged women to share their stories; I was honored by their trust and candidacy and awed by their sincere desire to support one another and prevent others from suffering in the future. I believe that the synergism of this bimodal approach addresses the complex challenge presented by obstetric fistula; by enlarging our body of knowledge, we can mobilize resources to both prevent and cure fistula. By fostering supportive communities and de-stigmatization, we can facilitate an environment in which women are able to heal.
OBJECTIVES

To determine a method for demonstrating pain reduction in hospitalized children using a quality outcome indicator; then to determine whether children had documented reductions in pain.

Methods: Utilized and modified a nationally known nursing quality process measure (Pediatric Pain Assessment/intervention/Reassessment Cycle) to determine if children get pain relief. Using 24-hour retrospective chart review, nurses in 4 children’s hospitals collected data about the pain experience for children on either medical or surgical units. Data collected included pain scale scores on initial assessment and after an intervention, length of time to reassessment after an intervention, gender and age of child, type of pain, type of pain scale used, and type of intervention used. Per cent reductions in pain for all children’s pain scores greater than 0 were calculated and data analyzed using exploratory descriptive statistics.

RESULTS

Sample size consisted of 101 children between 3-19 years of age with complete data for PAIR cycle; 41 children had pain scores greater than 0, 1/3 female and 2/3 male. Half of the children with documented pain were adolescents while the other fifty percent split roughly between preschool and school age children. Relief of pain was deemed significant if reduced by at least 20% on a pain scale equivalent of 1-10. Mean pain scale score was 4.66; 61% had a reduction in pain of at least 20%, 39% did not. 82% of preschool and 83% of school age children had at least 10% reduction in pain while only 42% of adolescents (who tended to self-report their pain scores) had any relief. Pharmacologic interventions were used in 73% of children with pain; minimal use was made of other interventions. Time to reassessment of pain after intervention varied widely from 30 minutes to 6 hours or more. Children with higher documented pain scores were less likely than children with lower scores to get at least 20% reduction in pain.

RECOMMENDATIONS

Drive development of national standards and institutional policies to reduce times to reassessment after pain intervention; increase nurses’ knowledge of appropriate pain scales for each age child and type of pain; increase nurses’ knowledge of a wide variety of pain-relieving interventions and study effectiveness of each; leverage use of a large national database to drive collection and examination of pain management processes and reductions in pain for hospitalized children through an outcome measure such as the one employed in this study.
How Individual Providers Change Practice: A Grounded Theory Study of Maternity Care Practitioners and Delayed Cord Cutting

OBJECTIVES/BACKGROUND
Improving evidence-based care often requires providers to change practices, yet studies show that change initiatives at the organizational level are often ineffective. This has been especially true in maternity care. The phenomenon of individual provider change of practice toward more evidence-based forms of care has rarely been investigated. This study was conducted to explore the experiences of maternity care practitioners (physicians and midwives) who decided to change practice from early umbilical cord clamping after delivery, to delayed umbilical cord clamping.

METHODS
This was a qualitative, grounded theory study using semi-structured interviews. Atlas.Ti 6.0 software was used during the analysis phase. Data collection and analysis took place between June 2011 and January 2012. Seventeen maternity care providers who met the inclusion criteria were interviewed.

RESULTS
The participants did not describe ‘deciding to change’ as much as they described an ‘evolution toward change’. Four emergent themes were found. These themes could also be seen as ‘drivers of change’. The themes were 1) trusting colleagues, 2) believing the evidence, 3) honoring families, and 4) preserving the integrity of the mother and baby. The only theme which served as a single driver of change was ‘honoring families’. Providers usually required 2 or more ‘drivers’ in their process of change. The most common combination was ‘trusting colleagues’ and ‘believing the evidence’. While ‘trusting colleagues’ was a strong factor in driving change, many participants reported hesitating speaking to colleagues about changing practice – suggesting a gap between what was effective for them and their willingness to be effective in supporting others to change practice. In addition, three ‘domains of influence’ were identified and populated by factors from the participants. These were the ‘personal domain’, the ‘professional domain’, and the ‘institutional domain’.

CONCLUSIONS
The Transformational Practice Change Model was developed to describe the phenomenon of individual provider change of practice. Three phases include Moving Toward Change, Integrating Change and Identifying with Change. The qualities of modularity, malleability, and non-linearity are commonly present when individuals progress through a change of practice. Some will make this change quickly and for some it may take months, even years. Understanding the nature of individual change may shed light on how larger change initiatives may be more successful.
Reproductive Health Training Curriculum for Indian Female Sex Workers

OBJECTIVES
Female Community Sex Workers (FCSWs) in India represent a vulnerable segment of the population due to the nature of their work. Young women in this line of work lack basic knowledge on their reproductive health as they progress through different stages of their life, particularly in relation to the menstruation cycle, menopause and breast cancer. Aastha Parivaar (AP), is a body of community organizations, formed to address HIV/AIDS and health related community needs among female sex workers in Mumbai and Thane. The purpose of this project was to develop a culturally appropriate health curriculum and training materials for peer-led health trainings among sex workers.

METHODS
The Aastha Parivaar student team began with a literature review of health indicators in India with a focus on women’s health. This review also explored existing educational materials currently used by organizations working with sex workers. The team established contact with AP to determine the type of training materials their organization desired to help facilitate their educational efforts. Their request for training materials on menstruation, breast cancer, and menopause ultimately led to the division of our team into three separate groups corresponding with each topic. Each group researched existing training materials available for women in the United States and then tailored the materials for the target population.

RESULTS
Given the vast amount of information that could be discussed with female sex workers regarding their reproductive health, the scope of work was narrowed down to include three sections: menstruation, breast cancer, and menopause. The final product is a comprehensive set of training materials to aid female community sex workers in Mumbai and Thane to understand their reproductive health systems, enabling them to lead healthier lives.

CONCLUSIONS
The peer, or lay health worker model has been widely used across a number of health topics to make significant improvements in health. Application of this model to community sex workers with little to no exposure to health education should serve as an appropriate introduction to a peer-led curriculum addressing key subject areas such as reproductive health in a culturally relevant manner. As this curriculum is implemented, facilitators may be able to adapt the teaching module and expand it to include additional female audiences or new health topics.
SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES

Provider Awareness, Knowledge and Perceptions of Text4baby in Washington, DC

BACKGROUND

Text4baby is a free health text messaging service that provides pregnant and new moms with accurate information about caring for themselves and their babies. With this program, text4baby aims to demonstrate the potential of mobile health technology in maternal and child health, and in reaching under-served populations with critical health information.

OBJECTIVE

This project will assess knowledge and use of text4baby among prenatal care providers in Wards 4, 5, 7, and 8, in the District of Columbia. This project will provide valuable information to expand the reach of the program through a greater understanding of provider knowledge and perceptions of the program, as well as perceptions and satisfaction of the program among current t4b partners.

METHODS

This project will conduct formative research on the text4baby program in Washington, DC utilizing both quantitative and qualitative methods. A sample of 70 prenatal healthcare providers in Wards 4, 5, 7, and 8 will be recruited to participate in an anonymous, online survey. Participants will be recruited via phone calls to the health centers, in order to obtain staff email addresses. Staff will then be emailed a link to the online survey. The online survey will assess awareness and knowledge of text4baby, perceptions about the text4baby program, and willingness to promote text4baby in their clinic. A second sample of 6-7 text4baby partners will be recruited via phone calls to primary contacts as identified by text4baby staff. A phone or in-person interview will be conducted with each respondent to assess perceptions of its effectiveness, barriers to increasing enrollment, and implementation issues.

RESULTS TO DATE

Both descriptive qualitative and quantitative analysis will be performed. The online survey results will be analyzed using SPSS software. The in-depth interview data will be analyzed using NVIVO software.

CONCLUSION

Recommendations will be made to text4baby to enable staff to make improvements, and better educate providers about the program in order to increase enrollment rates and hopefully improve birth outcomes.
Effectiveness of Text4Baby Flu Vaccination Reminder Module

We will conduct phone surveys with subscribers of the text4baby system who received a flu shot after getting a series of reminder texts. The goals of this study were to gather information about the text4baby audience’s history and future plans to get the flu shot, motivations and barriers to obtaining flu shots and how they overcame those barriers, feelings about getting the flu shot in the past, and responsiveness to the reminder system and the interactive component to text4baby. After surveying 30-50 participants, the data will be analyzed using SPSS to determine correlations between the flu reminder system and the knowledge, attitudes, and behaviors of the participants. Results are pending completion of survey analysis.
Women’s/Child Health

School of Public Health and Health Services
A Health Needs Assessment of Arab-Americans in the Washington, DC Area

Background
Arab-Americans often face various health challenges due to the trauma and stress associated with immigration, cultural conflict in the US, loss of social support, and limited knowledge of the complex U.S. health system. However, there is a paucity of research examining health risks and behaviors among this ethnic group.

Objectives
This project will assess the health needs among Arab-Americans living in the Washington, DC metropolitan area.

Methods
This cross-sectional study will use a non-probability, convenience sample of Arab-Americans living in the Washington, D.C. metropolitan area. The sample will include 150 English-proficient men and women 18 years and older who self-identify as Arab-American or of Arab descent. Participants will be recruited to take the online survey via e-mail listserves, social networking sites, and from a previous sample of participants from a cardiovascular disease study. Specifically, it will examine health care access and utilization, perceptions of health issues, risk behaviors, and health status among Arab-Americans adults. The study will also measure for associations between reported stress, perceived discrimination, acculturation, and health.

Results
Quantitative analysis will be conducted using SPSS 19.0 including overall frequencies, cross-tabulations by socio-demographic factors; analysis of variance examining the relationships between acculturation, discrimination, stress, and health status.

Conclusion
Information collected from this research will be gathered to design and eventually implement health promotion programs for Arabs and Arab-Americans in the DC metropolitan area, based on the needs of this community.
Text4Baby Message Content and Promotional Material Perception Among Latina Women in Washington, DC

BACKGROUND

Text4Baby (T4B) is a National campaign that uses mobile health as a platform to increase knowledge and frequency of positive health behaviors relevant to pregnant and new mothers. Based off of research conducted by the National Latino Research Center in San Diego, currently 6% of T4B users use the Spanish version of T4B, which is the lowest participating population.

OBJECTIVE

To assess the perception of current T4B Spanish message content of ten health messages and current promotional material focused towards Latina women living in Washington, DC.

METHODS

A sample of Latina women participating in T4B will be recruited through Mary’s Center in Washington, DC. Recruitment will be done through current T4B users among Mary’s Center Health Clinic. The sample size will consist of thirty-two women. Four focus groups of eight women will be conducted over a six-week period. Focus groups will include questions pertaining to feedback on the appropriateness of ten specific messages concerning tone and translation, effectiveness of current T4B promotional material, and potential future recruitment strategies.

RESULTS

NVivo will be used to assess the qualitative data focus group data concerning the perceptions of Spanish language message content and promotional material pertaining to T4B health messages.

CONCLUSION

By conducting qualitative research through focus groups in Latina women living in Washington, DC, better strategies can be developed to increase T4B recruitment, and current message content perceptions on health information.
WOMEN’S/CHILD HEALTH

SCHOOL OF PUBLIC HEALTH AND HEALTH SERVICES
Expectant and New Mothers Knowledge of Text4Baby in Washington, DC

OBJECTIVE
This project will assess pregnant and new mother’s knowledge of the Text4Baby program in Washington, DC. The Text4Baby program is a national free health text messaging service in English and Spanish for new and expectant mothers. Its goal is to increase healthy birth outcomes and decrease the incidence of low birth weight and other negative birth outcomes. This project will conduct a quantitative survey to better understand 1) exposure of the program among new and expectant mothers in Washington, DC, 2) barriers to use of the program among non-users and users; and 3) perceptions of the program among current users.

METHODS
A quantitative survey of 75 mothers will be conducted. Expectant and new mothers will be recruited from clinics and practices throughout Washington, DC. Flyers will be distributed and posted in clinic waiting rooms and eligible participants will be given a paper/pencil survey to be completed in the waiting room. Women who complete the survey will be given a $10 gift card as an incentive to take the survey as they were waiting for their appointment. All survey data will be entered into SPSS for analysis.

RESULTS
Descriptive and bivariate analysis will be conducted to examine overall exposure to the program, barriers to enrollment, and perceptions of the program. Further analysis will examine relationships between sociodemographics, due date or newborn age and exposure and perceptions.

CONCLUSION
This project will help provide critical insight into the use of Text4Baby and perceptions of the program. Recommendations will be made to Text4Baby about how to better reach expectant and new mothers to increase enrollment for the free text messaging service to improve birth outcomes.
START OF DAY TWO
ANNUAL RESEARCH DAY
Thursday, March 29, 2012

Marvin Center – 800 21st Street, NW

8:00 – 9:00 A.M.
Registration and Breakfast

Posters to be Mounted on Posterboards

9:00 A.M. – 12:00 P.M.
Poster Session and Judging

12:00 – 1:30 P.M.
Lunch & Poster Removal

Media and Public Affairs Building, Jack Morton Auditorium – 805 21st Street, NW

1:30 – 1:35 P.M.
Introduction of Keynote Speaker
Dr. Leo M. Chalupa, Ph.D.
Vice President for Research

1:35 – 3:00 P.M.
Keynote Address
Alan Leshner, Ph.D.
CEO, American Association for the Advancement of Science
“Science in the 2012 Climate”

Award Ceremony
Dr. Steven Lerman, Ph.D.
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Environmental Sustainability and Business

With the rising global awareness towards environmental sustainability, the automobile industry has implemented the production of hybrid, plug-in hybrid, and electric cars. For taxicab companies such as EnviroCAB in Arlington, Virginia, a new consideration can be taken: should they invest in, purchase, and drive more environmentally friendly vehicles? EnviroCAB, founded in 2007, has already established itself as an environmentally friendly company, claiming that its 50 all-hybrid vehicles comprise the “world’s first carbon-negative taxi fleet.”

This research project studies the various business possibilities EnviroCAB can consider. EnviroCAB can enable the inclusion of plug-in hybrid and electric taxicabs into its current fleet. With these myriad business alternatives, the research case provides the foundation for the cost-benefit analyses of factors such as automobile cost, fuel economy, cargo space, battery power output, and more. The integration of new, more environmentally friendly cars, however, comes with the cost of higher manufacturer’s suggested retail prices and a business risk. The case study gives an in-depth review of EnviroCAB’s current all-hybrid fleet, the taxicab’s competition, information on the plug-in and pure electric cars, as well as the marketing questions that can be considered for EnviroCAB.
With the rising global awareness towards environmental sustainability, the automobile industry has implemented the production of hybrid, plug-in hybrid, and electric cars. Electric vehicles are the trend of the future. Three main advantages are low CO2 emission, low operational cost and low gas consumption. Many people believe governments should be early adopters of these cars, setting a positive example of environmental sustainability for local residents. The D.C. government has always been a leader in green campaigns. Should it replace conventional vehicles with electric vehicles in 2012?

The research project studies the current situation of the D.C. fleet management team and various factors that might affect administrators to make a decision. All of the useful information is presented as part of a conversation. With these complicated management elements, the research case provides the foundation for the cost-benefit analyses of factors such as initial and operational cost, local charging infrastructure, gas prices, battery performance and more. The integration of electric vehicles, however, comes with challenges for the present fleet management team, such as maintenance skills required for mechanics. The case study gives an in-depth review of considerations from relevant department leaders on purchasing electric cars, as well as the long-term city plan that need to be thought about before the purchasing decision.
The impact of government policies on the productivity of manufacturing firms: evidence from Eastern Europe and Central Asia between 1995 and 2009

This study investigates whether trade-related targeted government policies have had an impact on the total factor productivity (TFP) of manufacturing firms in Eastern Europe and Central Asia between 1995 and 2009. It does so by looking at how different types of primarily industry-specific trade policies (or their combinations) impact firm productivity, and subsequent economic growth. It also examines how industry-specific trade policies impact firm-level productivity depending on various investment climate characteristics, such as corruption, access to finance, physical infrastructure, and innovation.

The dependent variable is firm total factor productivity (TFP) calculated using the Levinsohn-Petrin approach. As an alternative measure of firm productivity, this study uses the labor productivity. Similar to Bastos and Nazir (2004), this research utilizes the Principal Component Analysis to group certain investment climate indicators.

To conclude, this research addresses a gap in the literature by disaggregating the effects of different types of trade policies (or their combinations) on firm productivity in developing and emerging markets. It also explores the impact that the interaction between the trade-related reforms and the basic investment climate variables has on performance of manufacturing firms in developing and emerging markets.
COLUMBIAN COLLEGE OF ARTS & SCIENCES

Dance in Ghana: A Progressive Force Grounded in Tradition

I received a Luther Rice fellowship in order to fund the research I conducted while abroad in Ghana last semester. Essentially, I answered the following three questions: In a nation where dance plays an integral role in daily affairs and is a highly respected art form, how are Ghanaians employing dance as a means of preserving their history and remaining true to their cultural art form, while also reflecting contemporary developments and attitudes towards dance? How are they able to foster rich international exchanges with dance communities and institutions around the world with these progressive and true-to-form Ghanaian works? How can the Ghanaian choreographers’ ability to modernize their traditional dances serve as a model for me as a young choreographer to use my training as a modern and classical Indian dancer to create dances addressing contemporary developments while remaining true to my style of movement? In order to answer these questions, I enrolled in two traditional dance classes at the University of Ghana’s School of Performing Arts as well as a drumming class. I conducted interviews with my classmates, teaching assistants, master’s students, professors, and professional dancers and choreographers. I am currently working on assembling my results into a video documentary and a poster presentation.
The Bard's Brother: The Influence of Edmund Shakespeare and Family

Through the generosity of The George Washington University George Gamow Undergraduate Research Award, I was able to travel to London for one week in November of 2011 to study Edmund Shakespeare—the youngest sibling of playwright William Shakespeare. Very little is known of the Bard's brother, but the limited evidence we possess begins to paint the picture of a young, foolish man desperate to follow in his elder brother's footsteps. To further develop his character, the Undergraduate Research Office accepted my proposal to write a full length play revolving around the supposed relationship of the brothers and Edmund's possible influence over one of William's greatest works: King Lear.

After having gathered research from various sites and organizations in London and the Shakespeare's hometown of Stratford-Upon-Avon, I present the assumption that both brothers fought to obtain the praise of their overly ambitious father, John. William must have been deemed the favorite child. He possessed a mind for Latin and literature that could potentially lead him to the finest universities in England, a path his eager father could only dream of. He would later earn enough money to purchase the largest property in Stratford and a coat of arms to bear his father's precious family name. Edmund, the youngest and least educated, was left behind.

Edmund followed William to London at an unknown date, fathered a bastard son, and died an actor. My research and final play will fill in the many gaps surrounding his life, in particular his final two years between 1605 and 1607. Many of William Shakespeare's works contain feuding and spiteful siblings. I present the assumption that Edmund inspired this trend.
Deliberate Untruths

Things fall apart so easily when they have been held together with lies.

Movement has commonly been used as a means to express human emotion, and as an outlet for the feelings associated with them. This work explores the human action of lying, its effects on a person internally, externally, the events in their lives, and their relationships with others. By interpreting through movement how people lie in a social setting, lie to get what they want, lie to please others, lie about their sexuality, lie about their feelings, and lie to themselves, I have created a work that all audience members can relate to in some aspect. This movement was generated organically, by pulling original movement from the cast’s improvisations on the different areas in lying and how they felt and related towards them. Gestures such as covering the face with both hands, contorting the body and locking away the arms behind show the nature of lies; it shows how they can destroy us from the inside out.
CREATIVE ARTS

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GW Interior Design Program’s Participation in the U.S. Department of Energy’s Solar Decathlon 2013

The Interior Design Program is conducting a course during the Spring 2012 semester for graduate and undergraduate students to design a solar-powered home with The Catholic University of American School of Architecture and Planning. A collaborative and multi-disciplinary team of including the GW School of Engineering and Applied Science (which has contributed to the design of the structural frame as well as the photovoltaic system), GW Landscaping and American University graphic design students are competing under the name Team Capitol DC in the 2013 Solar Decathlon. This competition, held every two years, is sponsored by The U.S. Department of Energy, which “Challenges collegiate teams to design, build, and operate solar-powered houses that are cost-effective, energy-efficient, and attractive. The winner of the competition is the team that best blends affordability, consumer appeal, and design excellence with optimal energy production and maximum efficiency.”

The Interior Design Program course interfaces with the architecture and is exploring how the inhabitants of the house will work, live, play, and sleep. In addition to studying the functions of the spaces and designing them, a study of lighting, materials, furnishings, ADA accessibility, and equipment is being thoroughly investigated under the lens of sustainability as well as affordability.
Four years ago Plan 3000, a marginalized community outside of the city of Santa Cruz, Bolivia began the fight for its own university. The first students of the Universidad Popular Igualitaria Andrés Ibáñez (UPIAI) are entering their sixth semester, yet the law dictating the legal functioning of the University still has not been passed. Lack of funding and government support have hindered the community’s ability to make their dreams for accessible higher education a reality. All of the activists involved in the creation of UPIAI are seriously aware of the connection between education and development and feel that the lack of higher education in their community has marginalized the youth of Plan 3000 and the community at large. Despite various setbacks, the students, teachers and administrators of UPIAI continue to fight for the University, with hopes that it will form leaders that can bring positive social change to Plan 3000 and all of Bolivia.
Traditionally, natural resources have defined the economic success of a nation. Today however, nations that lack this advantage are turning to their human capital as a means of bridging the development gap. The purpose of this research paper is to evaluate how the United States, Singapore and other ASEAN Nations utilize technology, media and formal distance learning programs, to develop their intellectual capital.

While there is an abundance of research into the practices of individual countries and their effects, few studies have taken the next step of comparative evaluation. For example, PISA (2010) has shown that Singapore is out-competing many developed nations, to the point where the US is attempting to mirror its middle school structure (Teo, 2009), but no significant study has asked or answered how these approaches compare.

This paper’s comparative approach will be used to not only find effective program implementations and best practices but also provide scaffoldings for other nations. A historical analysis will be used to relate the nations’ use of technology and distance learning to promote their economy. By utilizing this approach, key differences between the program structure and methodologies can be seen, as well as facilitating a critical analysis of the policy borrowing that has occurred.

This paper will examine the effectiveness of the programs against student achievement, common perceptions and the growth of intellectual resources. The paper will discuss the necessary elements of successful technology and media programme implementations in South and East Asia.
The Human Services Education: How does it meet the needs of the Human Services Field?

The scope of the Human Services field encompasses professional spheres from advocacy to social work, public welfare to education and much more. Although the field spans multiple sectors and specializations, it is tied together with a common purpose: to respond to human needs in order to help people live better lives. The fact that the field is constantly evolving as human needs change coupled with the variation within the field creates a challenge for educational institutions preparing Human Services professionals. Thus, the purpose of this research is to explore how human services education programs strive to meet the needs of the diverse and ever-changing field for which they are named.

This research includes a discussion of modern interpretations of the meaning of Human Services as depicted by existing literature. Literature also lends to a conversation about the shifting needs of the field, the factors that shape these needs and the theories and methods of existing Human Services degree programs. Informed by the literature, this study includes a qualitative interview conducted with Karen Key, the Vice President of Programs at the National Human Services Assembly. In addition, archival data in the form of transcripts from individual interviews with alumni from Human Services program were analyzed in order to gain an understanding of how a particular program strives to address the needs of the field. Initial findings from this research reveal themes including the need for increased visibility for human services education programs on multiple levels. Additionally, the possibilities for and rewards of mutually beneficial relationships between universities and human services institutions come to light. The importance of a strong infrastructure supporting Human Services Education programs also emerges. These and others will be discussed at length after further analysis of the data and literature.
The purpose of this study is to understand the perceptions and experiences of undergraduate student tutors as it pertains to the recognition and cultivation among their tutees’ leadership abilities. At many undergraduate institutions, there are often opportunities for students to tutor minority students in grades K – 8 through various academic enrichment programs. Few studies have sought to understand the role of leadership recognition and cultivation in minority tutees. Using the relational leadership model as both philosophical and practical base, this exploratory study examines student tutors’ understanding of leadership related to the students with whom they work. Participants for the study were selected from three DC Reads academic enrichment programs at The George Washington University. Initial findings reveal that leadership recognition and cultivation plays a key role in the development and future of tutees’ outcomes. In addition, the study advises different methods for instruction and learning.
Establishing the foundation: Urban women literacy project

The initial ideas for this project were created for the 2012 Clinton Global Initiative University. The purpose is to understand how adult literacy programs in Washington, D.C. function and serve people. This study is part of a larger goal to develop an organization to encourage women to become literate.

Almost 20 percent of the global population (more than 774 million young people and adults) lack basic literacy skills (Richmond et al, 2008). Without these skills, people cannot be fully engaged in society. Literate people have the opportunity to contribute to basic needs, such as maintaining a bank account or applying for jobs. People who are literate can express their concerns and gather an understanding of their environment. Literacy is a human right. More than 60 percent of the population that lacks literacy skills is female. While the United States fares better than other countries (CIA Worldfactbook, 2011), there are a number of areas in the U.S. that deserve attention (http://nces.ed.gov/naal/estimates).

Koichiro Matsuura, Director General of United Nations Educational, Scientific and Cultural Organization (UNESCO) stated: "Literacy is about empowerment. It increases awareness …influences the behavior of individuals, families and communities…improves communication skills, gives access to knowledge and builds the self-confidence and self-esteem needed to make decisions" (in Richmond et al., 2008, p. 21).

The author intends to conduct a qualitative study, with interviews, document analysis and observations to explore approximately four local organizations. This project is scheduled to start in Summer 2012. Results are to be determined. The author hopes to understand how adult literacy programs in an urban area operate and develop people in the community.
Neuropsychological and Behavioral Outcomes of Late Preterm Birth Following In Vitro Fertilization

OBJECTIVE

Fewer behavior problems, higher academic achievement scores, and better verbal ability have been reported in children conceived by in vitro fertilization (IVF). However, the literature is inconsistent about whether IVF is a neutral, advantageous, or negative psychological factor for late preterm children (LPT; 34-36 gestational weeks). This study was conducted to determine the extent to which IVF conception influences neuropsychological and behavioral outcomes in a single-center cohort of three-year-old children born preterm between 2004-2007.

METHOD

Participants were 273 LPT children (mean age= 3.8) grouped by conception method: 1) IVF; n=77 (35 male/42 female) 2) non-IVF; n=196 (108 male/88 female). General conceptual ability (GCA), nonverbal reasoning, visual-spatial and visual-motor skill, manual dexterity, selective attention, executive function, and learning/memory were assessed, and parental behavioral and executive function questionnaires completed.

RESULTS

Differences were found for maternal age (IVF=37.6; non-IVF=33.2; p<.001) and birth weight (IVF=2316.7g; non-IVF=2539.0g; p<.001), but not intelligence (IVF/GCA=105.4; non-IVF/GCA=107.3). ANOVAs indicated no group differences in any cognitive, neuropsychological, or behavioral variable except parental anxiety ratings, which were lower for IVF than non-IVF (p=.048), but no longer significant after covarying for maternal age, birth weight, and gender.

CONCLUSION

IVF appeared to be a neutral factor that did not increase risk of general cognitive, neuropsychological, or behavioral impairment in our LPT preschoolers. Longitudinal study of LPT children at elementary school age may detect subtle impairments not apparent at age three due to advancing maturity of subjects and better ability to perform discriminatory testing, specifically for executive function.
EDUCATION

COLUMBIAN COLLEGE OF ARTS & SCIENCES

Multiple Instrumental Case Studies of Inclusive STEM-focused High Schools: Opportunity Structures for Preparation and Inspiration

This presentation represents student work done for the NSF funded project “Multiple Instrumental Case Studies of Inclusive STEM-focused High Schools: Opportunity Structures for Preparation and Inspiration.” The principle investigator for that project is Sharon Lynch (GW) and the co-PIs are Tara Behrend (GW), Erin Peters Burton (GMU), and Barbara Means (SRI).

As the US seeks to maintain a powerful role in our world’s science, mathematics and technology endeavors, new programs are being created to form the next generation of STEM professionals. In 2010, President Obama issued a challenge to the U.S. education system to create more than 1000 new STEM-focused schools over the next decade, including 200 high schools. The current study focuses on a new type of school emerging across the US, Inclusive STEM-focused High Schools (ISHSs). Unlike selective STEM-focused schools that target students already identified as STEM talented, ISHSs seek to develop new sources of STEM talent among under-represented minority students and provide them with the means to succeed in school, STEM jobs, college majors, and careers (Means, Confrey, House, & Bhanot, 2008; Scott, 2009). However, ISHSs are a new phenomenon and their ability to meet their goals has not been well documented in the research literature. The current study aims to develop a body of evidence to identify the critical components of ISHSs and propose a common theory of action. The study has identified 10 critical components that guide ISHSs ranging from students’ academic success to use of technology to structural organization of the program. We will be visiting Manor New Technology High School in East Manor, Texas this upcoming May as the first visit of several to well-established “exemplar” ISHSs to assess student STEM outcomes for each ISHS compared with school district and state means by studying their designs and implementations in their varied contexts. Unlike coverage of alternative schools by the popular media that suggests that any alternative is superior to the comprehensive school counterpart, the study should assist educators and policymakers in making decisions about ISHSs and their potential to increase the pool of STEM-prepared and inspired students.
The researches on writing in a Chinese as a foreign language (CFL) are still preliminary. This action research aims at how using the writing process facilitates CFL students’ writing and speaking in the presentational mode. College-level CFL students at Intermediate-mid level according to the American Council of Teaching Foreign Languages (ACTFL) standards, write a term project with the topic of comparison between Americans (or their home countrymen) and Chinese on a particular issue. Students are suggested that they follow the structure of a previous written a miniature Chinese composition in one of their take-home tests. Students have to complete this term project in a group of four, decide on the topic, write a composition, have at least two relevant questions for discussion, and make a presentation with PowerPoint in class for writer’s theater. As the following chart, there are four phases they need to complete. Meanwhile, checklists and grading rubric are provided to remind students of their writing process.

<table>
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<tr>
<th>Phase</th>
<th>Due date</th>
<th>Writing Process Stage</th>
<th>Weighted percentage</th>
<th>Focus of Group Work</th>
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<tr>
<td>1</td>
<td>3/1</td>
<td>Prewriting/drafting</td>
<td>10%</td>
<td>Brainstorming, semantic mapping; focus on ideas and organization</td>
</tr>
<tr>
<td>2</td>
<td>3/20</td>
<td>Revising/editing</td>
<td>20%</td>
<td>Paragraph writing; focus on voice/word choice/sentence fluency</td>
</tr>
<tr>
<td>3</td>
<td>4/3</td>
<td>Proofreading</td>
<td>30%</td>
<td>Working toward completion; to be submitted with PowerPoint in which at least 2 questions for discussions included; focus on sentence fluency/conventions/mechanics</td>
</tr>
<tr>
<td>4</td>
<td>4/30 &amp; 5/1</td>
<td>Publishing</td>
<td>40%</td>
<td>Presentational mode; focus on speaking and discussion orally in a revised reader’s theater</td>
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The following questions are to be answered:

What are students’ perceptions of:

a. Whether using the writing process collaboratively to write a composition in Chinese helps them better organize and express their ideas; and

b. Whether using the rubric and checklists help them improve the quality of their Chinese writing.

Questionnaires and interviews will be used to collect data.
A Multidisciplinary Approach to Early Childhood Development Doctoral Level Curriculum Development

This project details the developmental process of a doctoral level course curriculum on early childhood typical and atypical development. The curriculum was constructed to build a community of doctoral students who in working together develop a critical approach to the theoretical perspectives that currently define and describe the course of child growth and development, typicality and atypicality, risk and resilience in the early years. The final curriculum presents opportunities for each student to become familiar with the related neuroscience research and the possibilities of its application in understanding the developmental course of the young child. And, the course is designed to build a deeper understanding of the variance in human development and how the most at risk and vulnerable children can be carefully and effectively served.
Edu-preneurship Strategies for Underrepresented Graduate & Doctoral Student Success

Recently Dr. Freeman Hrabowski, President of the University of Maryland Baltimore County stated, “It’s easier to get a camel through the eye of a needle than to get a minority through a PhD program” (2012). Using online survey data collected from 108 participants over two-weeks using snowball sampling, specific challenges that are common to underrepresented graduate and doctoral students emerged from the data. These challenges include: “academic hazing” treatment in lieu of direct and engaging academic support; lack of external accountability measures; time, project, and life management strategies; lack of visible mentors; social capital in the form of “the unwritten rules to completing the doctorate”; and individual and institutional racism. In response to the emerging themes from my study, I am proposing a comprehensive ‘edu-preneurship’ business model entitled Gold Mind, LLC to serve as a companion to graduate and doctoral students by providing strategic, simple, step-by-step solutions for success. The values of the Gold Mind will include commitments to 1) working with graduate and doctoral students who may or may not pursue full-time faculty roles, 2) working with graduate and doctoral students who have various perspectives concerning employment and academia including a scholar-practitioner approach, 3) work-life-academic integration opposed balance, 4) humble stewardship of graduate and doctoral education as a mutually beneficial resource to be shared, and 5) fully utilizing the usefulness of emerging technology, while also acknowledging its weaknesses. Solutions offered by Gold Mind may include individualized advising, tele-events, in-person events, cohort communities for special populations (such as women and minorities in STEM), training for university administrators, and social media learning communities such as ‘The Gold Ink Spot’ – an online blog community for emerging scholar-practitioners. Overall, Gold Mind utilizes the extant literature to provide an entrepreneurial response to the problematized experiences of minority doctoral students (Gildersleeve, Croom, & Vasquez, 2011).
SCHOOL OF ENGINEERING & APPLIED SCIENCE

Noninvasive monitoring and determination of arterial plaque burden by segmenting B-mode ultrasound images

BACKGROUND

The goal of this research is to establish a noninvasive, cost-efficient method for determining the degree of arterial narrowing in patients with arterial disease using only ultrasound images. Unlike current ultrasound methods for determining the degree of arterial stenosis, this method will use individual pixel characteristics to determine and define the plaque-intima boundary and plaque-lumen boundary to compute the plaque area and volume present within the imaged artery. Color flow duplex imaging is the current "gold standard" for noninvasive grading of arterial stenosis where grading arterial stenosis is based on the peak systolic velocity ratio. This, however, is not an exact determination of the degree of atherosclerotic plaque buildup, but rather is only an estimate of the degree of narrowing.

METHODS

Each image will be preprocessed before image analysis in the MATLAB environment to reduce noise and speckle inherent within the images. Each image will then undergo image segmentation, which is the partitioning of an image into pixel regions on the basis of pixel characteristics, to differentiate the plaque burden from the arterial wall and the blood. Segmenting the plaque burden from the surrounding tissue will allow area and volume determination to be carried out, providing a quantifiable measurement of the plaque burden within the diseased artery. We are currently working on obtaining access to patient ultrasound images of diseased and healthy carotid arteries.

RESULTS

From preliminary image analysis carried out on ultrasound images of the peripheral arteries it was determined that the process of image segmentation can successfully segment the plaque burden from the surrounding tissue. The segmentation results show the visual representation of the segmented plaque region. The area determination results provide a quantitative measurement of the plaque size. This area corresponds not to physical dimensions such as millimeters or centimeters, but the number of pixels included in the segmented region. Some quantitative data would be beneficial but given the preliminary nature of this work it is probably not possible to provide any numbers.

CONCLUSIONS

The proposed method may provide a more exact measurement of arterial plaque burden compared to color flow duplex imaging, and may also provide a noninvasive and cost efficient means to monitor and assess the effect that preventative medications, diet, and exercise have on plaque size.
An experimental swirling jet is created by independently controlling the axial and angular momentum injection with the resulting water jet discharging freely into a large tank. The jet is excited to enhance mixing in low to high swirl number regimes. Axial forcing on the jet is imposed for Strouhal numbers ranging from 0 to 15, Reynolds number from 1,000 to 10,000, and Swirl number from 0 to 1.3, where limited experimental data exists. The forcing amplitude is changed from 1 to 20 percent of the axial flow rate, while the azimuthal momentum injection stays constant. The resulting forcing creates a jet with varying swirl number. Swirling jets enhance the growth and mixing of fluids compared to non-swirling jets. This leads to a more complete combustion, chemical process mixing, lower plume temperatures, and reduction in pollutant emissions. This mixing can be improved further by forcing natural instabilities in the jet. These imposed disturbances are either axial, which generates vortex rings, or angular, which create more complex structures. Past research involving forcing with swirling jets resulted in limited findings due to the concentration of forcing in either axial or angular directions. In this study, a combination of both axial and angular forcing is implemented and offers insight into the complex flow structures of the swirling jet in the vortex breakdown region, as observed in the near and far field of the jet. The flow structures of forced and steady jets are observed using PLIF: azimuthal dye injection in the periphery of the jet shear layer helps identify flow structures, while dye injection in the jet allows testing the effect of forcing on entrainment.
Experimental Investigation of Laminar Boundary Layer Instability at the Free-Surface of a Jet

Shear instabilities induced by the relaxation of a laminar boundary layer at the free surface of a high speed liquid jet are investigated experimentally. Understanding how a jet can breakup or interact with the surrounding gas is useful for numerous applications involving transfer between liquid and gas (fuel injector, climate modeling, mixing...). Physical insights into these instabilities are gained by performing non-intrusive measurements of flow structure in the direct vicinity of the surface. The experimental results are a combination of surface visualization, planar laser induced fluorescence (PLIF), and particle image velocimetry (PIV). They suggest that 2D spanwise vortices in the shear layer play a major role in these instabilities by triggering 2D waves on the free surface as predicted by linear stability analysis. These vortices, however, are found to travel at different speed than the surface waves they initially created resulting in constructive interference with the waves and wave growth. The waves also appear to be involved in the phenomenon of air entrainment.
The Development of a Closed-Loop Flight Controller with Panel Method Integration for Gust Alleviation using Biomimetic Feathers on Aircraft Wings

The existence of gusting flows and turbulence has burdened the aerospace industry over the last century. During this time numerous passive and active gust alleviation systems (GAS) have been developed but limited success. However, to date, techniques used by birds have yet to be implemented. The development of a biomimetic closed-loop flight controller that integrates gust alleviation and flight control into a single distributed system, offers flight capabilities once considered unobtainable. Modern flight controllers predominantly rely on and respond to perturbations in the global states, resulting in rotation or displacement of the entire aircraft prior to the response. This bio-inspired GAS employs active deflection of electromechanical feathers that react to changes in the airflow, i.e. the local states. The GAS design is a skeletal wing structure with a network of feather-like panels installed on the wing’s surfaces, creating the airfoil profile and replacing the trailing-edge flaps. In this study, a dynamic model of the GAS-integrated wing is simulated to compute gust-induced disturbances. The system implements continuous adjustment to flap orientation to perform corrective responses to inbound gusts. MATLAB simulations, using a closed-loop LQR integrated with a 2D adaptive panel method, allow analysis of the morphing structure’s aerodynamic data. Non-linear and linear dynamic models of the GAS are compared to a traditional single control surface baseline wing. The feedback loops synthesized rely on inertial changes in the global states; however, variations in trailing edge flap configuration are compared. The bio-inspired system’s distributed control effort allows more efficient response to gusts than the traditional wing by minimizing the magnitude and duration of the airfoil’s deviation from its equilibrium position. Consequently, the GAS demonstrates enhancements to maneuverability and stability in turbulent intensive environments.
A Non Intrusive Technique for Thermal Profiling of a Non-Isothermal Fluid

Imaging a system is a primary technique in the study of fluids. Challenges arise however, when dealing with non-isothermal conditions, since optically distorted images are generated due to the refraction of light. Additionally, accurately measuring the temperature at different locations of such systems is difficult. Non-isothermal systems are encountered frequently in places such as thermal energy storage systems, nuclear reactors and ocean and atmospheric currents. As such, analyzing them is important. A new optical technique is being developed that addresses both concerns of dealing with such systems.

An experiment was set up where a laser beam was passed through a non-isothermal fluid, generated using a heating element. The fluorescence of the beam, caused by the presence of a fluorescent dye, was recorded with a high resolution camera.

A Gaussian curve fit was done on the intensity plot of the beam, allowing its trajectory to be traced with sub-pixel accuracy. The change in gradient of the beam and hence the index of refraction could be calculated. Owing to a one to one relation, the temperature change could also be derived and thus a thermal profile of the system could be generated. Metrics for optical distortion could be calculated from the beam deflection as well.

This work has improved on the techniques used in the past where the deflection was measured a certain distance from the heating zone, resulting in inaccuracies. Presently, work is being done incorporating a grid laser pattern instead of a single beam. Successful implementation of this technique will enable extending applicability of tools such as particle image velocimetry, to non-isothermal flows.

RELEVANT PRESENTATIONS
- GW School of Engineering Research & Development Showcase, February 2012
- Siemens High School Competition Finals, Washington, DC, December 2011
Novel Hydrothermally Treated Nanocrystalline Hydroxyapatite and Magnetically Synthesized Single-walled Carbon Nanotubes for Orthopedic Applications

To date, there are a strikingly growing number of patients who need various orthopedic implants. To cure those problems, traditional metal implants such as titanium were chosen for orthopedic applications due to their excellent mechanical properties and biological inertness. However, conventional orthopedic implants face many complications such as infection and implant loosening which may lead to implant failures. Since natural bone matrix are nanostructured, it is desirable to design a biologically inspired nanostructured coating that can turn conventional inert titanium surfaces into biomimetic active interfaces, thus enhance bone cell adhesion and osseointegration.

For this purpose, we designed a biomimetic nanostructured coating based on nanocrystalline hydroxyapatites (nHA) and single-walled carbon nanotubes (SWCNTs) on titanium. Specifically, nHA with good crystallinity and biomimetic dimensions were prepared via a wet chemistry method and hydrothermal treatment; and the SWCNTs were synthesized via an arc plasma method with (B-SWCNT) or without magnetic fields (N-SWCNT). TEM images showed that the hydrothermally treated nHA possessed regular rod-like nanocrystals and biomimetic nanostructure. In addition, the length of SWCNTs can be significantly increased under external magnetic fields when compared to nanotubes produced without magnetic fields. More importantly, our results demonstrated that both of the nHA and SWCNTs nanomaterials can enhance osteoblast (bone-forming cell) adhesion on titanium in vitro due to their excellent cytocompatibility and biomimetic nanoscale dimensions. Especially, co-coating nHA and SWCNTs together can achieve a synergic effect to greatly promote osteoblast adhesion, thus making them promising to improve the efficiency of traditional implants. In summary, this study provides a novel biologically inspired nano coating design for better osseointegration, thus worth further exploration.
COLUMBIAN COLLEGE OF ARTS & SCIENCES

Transgender Voice and Communication Treatment: A Retrospective Chart Review of 25 Cases

BACKGROUND

People transitioning from male to female (MTF) gender seek speech-language pathology services when they feel their voice is betraying their genuine self or perhaps is the last obstacle to representing their authentic gender. Speaking fundamental frequency (pitch) and resonance are most often targeted in treatment because the combination of these two voice characteristics can account for the majority of gender perception. Intonation, pragmatics, and non-verbal communication contribute to a lesser extent and are often recommended in treatment guidelines. There are few examples in the research literature of effective treatment.

METHODS

Demographic information and treatment outcome data (e.g., acoustic measures) were collected via chart review of 25 of the 32 cases discharged from The George Washington University Speech and Hearing Center between 2006 and 2010.

RESULTS

Clients were in various stages of male-to-female gender transitions during treatment: at discharge, 80% of them presented as female 100% of the time. A majority (88%) had a history of feminizing hormone treatment and 28% presented with a voice disorder separate from gender presentation concerns. Treatment goals included the following (listed in order of percentage of cases that addressed the topic): forward resonance, increased pitch, relaxation, intonation, phonotraumatic behaviors, breath control, non-verbal communication, pragmatics, and vocal hygiene. After treatment, clients had increased speaking fundamental frequency in sustained vowel, reading, and monologue tasks by 5-6 semitones, which is statistically significant. Gains in pitch correlated significantly with total number of sessions, but no other correlations were significant.

CONCLUSIONS

Treatment goals for these cases were consistent with those goals most often recommended in the research literature regarding voice and communication treatment for transgender clients. Voice and communication treatment resulted in gains in areas important to gender perception. Further research is warranted to determine efficacy of specific treatment protocols and potentially influential factors such as initial voice status.
Characterizing Postdoctoral Researchers and their Career Paths over time using NSF survey data

The National Science Foundation’s Survey of Doctorate Recipients is conducted every two or three years and collects detailed information on thousands of individuals receiving PhDs in science and engineering in the U.S. and some others with PhDs from abroad in these areas. A significant portion of the sample (e.g., 60% on 3 or more surveys from 1993-2006) appears in multiple survey years and can be linked across time. The surveys ask about postdoctoral experience and collect information on field of study, employment, managerial responsibilities, and demographics including marital status and children at home. In the U.S., women and minorities are severely underrepresented in many academic and nonacademic career areas of science, medicine, and engineering. This is a serious problem because women and minorities form a significant portion of the potential scientific workforce and maintaining a strong and vibrant scientific workforce is critical to economic and scientific progress. In this poster we present characteristics of the postdoctoral population over time based on the NSF SDR survey data. Survey weights adjust for oversampling of select groups and nonresponse on a cross sectional basis. Survey sampling methods are used to estimate standard errors associated with results. This research is funded by a cooperative agreement from the NIH National Institute of General Medical Sciences (NIGMS) on modeling the scientific workforce in health and medical sciences.
COLLEGE OF PROFESSIONAL STUDIES

An Exploratory, Longitudinal Analysis of Factors Influencing Neurologists' Distribution in The New York City Metropolitan Region, 1960-2010

OBJECTIVE

To conduct an exploratory analysis that identify factors that may affect the geographic distribution of neurologists between 1960 and 2010 in the greater New York City metropolitan region and to highlight the importance of conducting further investigations on neurologists' geographic distribution.

BACKGROUND

Newhouse et al. (1990, 2005), Politzer et al. (1991, 1998), and Ricketts and Randolph (2007) researched whether factors such as demographic indicators (population, median family income, etc) explained the distribution of primary care and board certified physicians from the 1960s through present. These studies used the American Medical Association's master file of physicians to analyze the urban-rural distribution of providers. Many factors including physician-population ratios and individual provider preference affect geographic distribution. To date, there is no analysis examining factors affecting the distribution of neurologists. Understanding what factors affect specialists' geographic distribution enables health service administrators predict the presence of specialists that will be available to provide specific services such as neurology and neurosurgery. By understanding what factors influence neurologists distribution, the authors believe developing predictive model will help to define workforce needs and better understand the impact on access to neurological services.

DESIGN/METHODS

To emphasize the focus on neurologists, the authors used the American Academy of Neurology directories and U.S. Census Bureau as the data sources. The data were examined over a fifty year time period (1960-2010). Nonparametric and simple regression models were established to determine if median family income and poverty levels affected the distribution of neurologists.

RESULTS

Combining the neurologist-to-population ratio growth rates with the trends in median family income and poverty levels, it appears that both income and poverty levels may influence neurologist distribution in the greater New York City metropolitan region.

CONCLUSIONS

The findings suggest that poverty and median income levels influence neurologists' geographic distribution pattern. The neurologists have followed the middle class population away from the center city. Further research is needed to understand other factors (access to research facilities, technology, etc.) affecting neurologists' distribution patterns and if the factors can formulate a model to predict neurologists' movements. As public health and health care leaders, it would be meaningful to understand the factors that influence neurologists' distribution in order to effectively plan for the community's needs.
The healthcare industry is constantly changing and transforming itself. To stay competitive, early careerists should find a mentor who can create opportunities for career advancement. The importance of a meaningful and successful mentor protégé relationship can yield lasting results and achievements. For example, the relationship will allow the protégé to establish oneself in a competitive job market and create networking opportunities. In return, protégés will be able to make contributions to their organization or professional growth – which in turn, indirectly, is the dividend to the mentor for the investment of time. Regardless of age or experience, having a mentor or learning how to mentor is an important part of becoming a well-rounded healthcare professional. There were six key techniques that have yielded a successful mentor-protégé relationship within the constraints Schmidt and Nguyen's long distance professional relationship:

1. Establish the Relationship
2. Create a Schedule
3. Create Expectations for each Meeting
4. Being Prepared to Discuss
5. Mentors Benefit as Well
6. Meet in Person

Mentoring relationships offer a number of important career benefits to the mentor and protégé. Organizations that do not have a structured and formal mentor-protégé program should consider establishing them, as protégés who foster a successful mentoring relationship will gain career and educational advancements.
Objective Measures of Anticipatory Anxiety in Adults Who Stutter

Anticipatory anxiety is central to certain theories of stuttering; increased anxiety is thought to precipitate stuttering moments. Anxiety can be measured objectively with heart rate (HR) and galvanic skin response (GSR), or subjectively with State Trait Anxiety Index (STAI). Findings on the stuttering-anxiety relationship are mixed, possibly due to different tasks and/or measures used across studies. There is a need to study anxiety and stuttering in ecologically valid tasks, as well as to measure anxiety immediate prior to, during, and after the stuttering moment. Our study compared HR and GSR in persons who stutter (PWS) before, during, and after stuttering moments while speaking in two virtual reality environments (VREs). Anticipatory anxiety theories predict higher levels of anxiety prior to a stutter when compared to during or after it.

**Method**

10 PWS gave two, 5-minute speeches (counterbalanced) in two VREs: with an audience and to an empty room. A total of n = 98 stutters, each with 5 seconds of fluent speech before and after their occurrence, were identified. GSR and HR were measured for the 5-second intervals prior to, during, and after each stutter. These were converted to percent change from baseline (%chbl) for each participant.

**Results**

A repeated measures MANOVA was used to analyze differences in %chbl for GSR and HR among the intervals. There were no significant differences or interactions between any of these intervals for either speaking task (i.e., audience or empty chairs). Changes in GSR and HR, before, during or after stuttering were not correlated with stuttering severity (SSI-4) or subjective reports of anxiety (STAI).

**Discussion**

Objective measures of anxiety do not change significantly prior to, during, and after a stuttering moment, a finding not predicted by anticipatory anxiety theories. Conversely, VREs may not be salient enough to detect differences in objective anxiety measures.
In October 2010, ten months after a 7.0 magnitude earthquake hit Haiti, a cholera outbreak began to further devastate the population. More than a year later, cholera has affected over 500,000 Haitians, over 5% of Haiti’s total population. Several epidemiological models published in March 2011 predicted the course of the epidemic and modeled potential intervention strategies. However, these models were based on data from early in the epidemic and therefore did not predict a secondary peak in cases during Haiti’s rainy season in late May 2011.

Our model builds on previous research but also incorporates current data and intervention strategies in order to provide updated predictions regarding endemic cholera in Haiti. Moreover, we seek to model a tertiary peak in the epidemic in May 2012 and provide insight into the mechanisms of endemic cholera in Haiti. To do this, we use a system of ordinary differential equations that includes a gravity term in order to express bacterial movement between regions. We started with testing various known models and parameter values for a best-fit model between the two regions experiencing the most cholera, namely, Ouest and Artibonite. We then model the relationships among all of the regions. Our goal is to forecast the effect of cholera’s rainy season on the epidemic using the data from the peak in May 2011 and predict another peak in May 2012.
Immune gene transcription profiling in Drosophila melanogaster infected with entomopathogenic nematodes and their symbiotic bacteria

Drosophila melanogaster is an excellent model for studying host-pathogen interactions and host innate immune responses. The Drosophila immune response is similar in many ways to mammalian immune response and flies share many physiological processes with mammalian hosts. Previous research in Drosophila has shown that flies use distinct mechanisms to respond to diverse pathogenic microorganisms such as bacteria, fungi and viruses. The most well studied Drosophila immune responses include the production of antimicrobial peptides, the activation of coagulation/melanization cascades in the blood, the synthesis of reactive oxygen species and the quick stimulation of hemocytes (equivalent to mammalian blood cells). However, Drosophila immune responses to parasitic organisms are not well understood. The current research involves a tripartite model consisting of Drosophila, the entomopathogenic (or insect pathogenic) nematode Heterorhabditis bacteriophora and its symbiotic bacterium Photobacterium luminescens. The great advantage of this model is that each partner of the Heterorhabditis/Photobacterium relationship can be separated and studied in isolation and in combinations, thus enabling the host immune responses against each player of the interaction to be studied alone or together. Previous studies have focused on virulence mechanisms that Photobacterium employs to kill insects. The main objective of this study is to investigate the molecular basis of Drosophila immune defense mechanisms against the bacteria and nematodes, separately or together. I have challenged Drosophila wild-type adult flies with Photobacterium alone, symbiotic nematodes (Heterorhabditis carrying Photobacterium) and axenic nematodes (Heterorhabditis lacking Photobacterium) and used quantitative RT-PCR to test the transcription of Drosophila immune-related genes at different time-points after the infection. Current results suggest that nematodes and bacteria elicit different immune gene transcription in flies. This research will shed light on the mechanisms used to fight bacterial and nematode infections in other insects that have dramatic repercussions on human life as agricultural pests or vectors of infectious diseases.
Application of Vibration Doppler Imaging in the Differentiation of Lesions in a Phantom Simulation

PURPOSE
The purpose of this study was to investigate the use of vibration Doppler imaging to differentiate lesions of varying composition.

MATERIALS AND METHODS
We constructed a tissue mimicking phantom into which we inserted objects of different consistencies to mimic lesions in liver tissue. To simulate a variety of lesions we used a pistachio without its shell, a pistachio with its shell, an olive, an olive seed, a seedless grape and a grape with a seed. We used a 7 MHz transducer and the vascular presets on a Phillips IU22 Ultrasound machine. The images were obtained in 4 sets namely: B-mode imaging, B-mode plus Power Doppler without vibration, Power Doppler with manual vibration (tapping on the container) and finally B-mode plus Power Doppler with higher frequency steady mechanical vibration (placing a phone vibrating at a constant frequency on top of the phantom).

RESULTS
We found that applying manual vibration to our simulated masses gave better definition to the borders of the “lesions” when compared to the images in plain B-mode imaging alone. Border definitions further improved when the higher frequency constant vibratory waves emitted from the cell phone were applied. With the higher frequency vibratory waves we were also able to better distinguish the internal textures of the “lesions” in comparison to both the plain B-mode imaging alone and when B-mode imaging was coupled with Power Doppler and manual vibration.

CONCLUSION
Vibration Doppler imaging improves the border definitions and internal textures of lesions of varying consistencies within a tissue mimicking phantom. We suggest that this technique of applying high frequency vibration during sonography holds much promise for improved sonographic assessment of solid lesions of varying composition.
The Role of Small RNA in HCV Infection and Downregulation of Tumor Suppressors

Based on the CDC’s current research, Hepatitis C Virus (HCV) is the most common chronic bloodborne infection in the U.S., infecting approximately 3.2 million people. With a rapid mutation rate (due to a high error rate of the virus’ RNA-dependent RNA polymerase) (1), it has been difficult to create an efficient and effective vaccine. It is commonly known that HCV infection can lead to Hepatocellular Carcinoma (HCC), a form of liver cancer (2). It is also commonly agreed upon that one of the most common causes of cancer is the loss of function of tumor suppressor genes (3). Therefore, one can infer that there may be a correlation between HCC and a loss of function in tumor suppressor genes. One of the most essential tumor suppressor genes is the PTEN (Phosphatase and tensin homolog) gene. Our research is focused on understanding the various mechanisms associated with HCV infection and downregulation of tumor suppressors like the PTEN gene (4,5). Through several molecular biological techniques, we are going to mutate RNA sequences of the virus, and assess its impact on the regulation of such tumor suppressors. With this knowledge, we hope to further comprehend the etiology of HCV infections and liver disease.

REFERENCES

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Because of their unique optical properties, surface-modified Gold and Silver Nanoparticles have found increased application for both detection and therapy in biotechnology. In this study, we have synthesized silver nanoparticles using a sodium citrate reduction reaction and have coated them with silica. The particles may be tagged with fluorescent dyes that are either intercalated into the porous silica ad-layer or covalently bound using a dye coupled through an amide bond. The structure of the modified nanoparticles has been verified through TEM imaging. Further, etching of the silver core using cyanide produces “nano-bubbles” whose structure can be confirmed through TEM but also through disappearance of the silver surface plasmon resonance feature in the absorption spectrum. Endocytosis into plant cells of the tagged-nanoparticles has been confirmed through confocal microscopy.
Prenatal Stress Alters Atherosclerotic Lesion Vulnerability in Adult Offspring

BACKGROUND

Chronic stress is a known risk factor for cardiovascular disease but the long-term effects of prenatal stress have not been well-studied. Recent data suggest that maternal stress is associated with larger atherosclerotic lesion area and a higher degree of endothelial dysfunction in offspring. We evaluated the effect of maternal stress on lesion size and vulnerability by measuring neovascularization and inflammation in adult offspring.

METHODS

Female ApoE knockout mice on a lard-containing diet were divided into stressed and non-stressed cages. Animals in the stressed group were subjected to chronic cold stress by placing them in 1 cm of iced water for 1 hour per day for the last 17 days of gestation. All offspring were sacrificed at 21 weeks of age. Atherosclerotic lesion score was determined, based on gross size, by a blinded observer examining the aortic arch. Atherosclerotic lesions in both the aortic sinus region and the aortic arch were stained with H&E, and Movats pentachrome. Macrophages were quantified in the aortic sinus region using Mac-2 staining.

RESULTS

In the aortic arch the prenatally stressed animals (n=7) had a greater lesion score, compared to the non-prenatally stressed group (n=8), indicating more apparent atherosclerotic lesions (P=0.026). In the aortic arch and branching vessels, plaque neovascularization was seen in 57% of the mice in the prenatally stressed group and in none of the animals in the non-stressed group (P=0.01). Animals subjected to prenatal stress had higher macrophage content in the aortic sinus lesions compared to non-prenatally stressed mice (p= 0.009).

CONCLUSIONS

In this animal model, prenatal stress is associated with larger lesions containing greater neovascularization in the aortic arch and branching vessels, and higher macrophage content in the aortic sinus lesions. These characteristics suggest that prenatal stress may lead to increased plaque vulnerability in adult offspring.
The George Washington University has always had ties to the African-American community, these connections date back to the school’s founding date on February 9, 1821. Whether it was through the slave labor that built its former campus called “College Hill” on Florida Avenue, the expulsion of Henry J. Arnold, a student trying to help slaves escape in 1847 or the graduation of its first African-American student, Samuel Laing Williams in 1884, 21 years after the first African-American graduated from Middlebury College, the university has developed a long and sometimes forgotten history with African-Americans.

This forgotten past has been replaced by contemporary accounts of segregation, blatant racism and an erased history of African-American students prior to Brown v Board of Education. Though African-American students faced discriminatory practices in the late 1800’s after Emancipation Proclamation, many of them were allowed entry into all-white institutions and were not denied solely based on race, as was the case in the in the early 20th century. However during the late 19th century, Columbian College served as a desired teaching ground for many of the District’s elite African-American families.

To aim of this project is to better understand this cultural academic shift, it is important to retrace the journey of African-American students who were pioneers at all-white colleges. Many white institutions similar to The George Washington University have had a storied history of African-American students. These students were the best and brightest of in their communities and their journey towards matriculation should be researched and celebrated.
Savage Sexism: Examining Gendered Intelligence in Hulk and She-Hulk Comics

My research aims to provide a thoughtful examination of the gendered social messages presented in Hulk and She-Hulk comics, and to raise meaningful questions about the ways in which She-Hulk differs from her cousin The Incredible Hulk. Faced with an absence of pre-existing scholarship, my research is meant to be viewed as a starting point from which scholars may explore the seemingly lost potential of She-Hulk’s intelligence, and ultimately bring to light problematic depictions of superheroines as seen in her comics. In addition to an analysis of Hulk and She-Hulk comics, this is done by synthesizing research from various fields, beginning with the economic arguments made by Matthew P. McAllister. McAllister’s idea that comics magnates’ drive for economic profit limits the content of comics and the opportunities for smaller companies to publish them sets the stage for a closer look at the gender differences in comic readership, and the content of She-Hulk comics. By utilizing results from a Russian study of children’s perceptions of intelligence, I discuss the extent to which intelligence is a sexually neutralizing element for Bruce Banner (Hulk) and Jennifer Walters (She-Hulk). Moving into a more visual analysis, I draw upon the research of Aaron Taylor to comment on superheroes’ issues with identity and body image in the context of the 1980s cult of fitness. Though She-Hulk is unique in her high intelligence and her ability to control her powers upon receiving them, what I ultimately (and unfortunately) find is that attempts at smashing the status quo are countered by the stereotypical sexism produced and perpetuated by patriarchy.
The Role of International Organizations in Humanitarian Crises

Humanitarian crises are complex situations that require a coordinated response from the international community. The involvement of international organizations in crisis situations is essential for ensuring that human dignity is respected and basic rights are upheld. However, despite repeated exposure to humanitarian crises, the collaborative effort of international organizations remains somewhat disorganized and at times ineffective. This paper offers a framework for the role of international organizations in humanitarian crises by identifying working definitions elemental to humanitarian aid work and analyzing existing scholarship regarding this field. From this foundation the paper will discuss the strengths and challenges of humanitarian intervention. The analysis of qualitative interviews of professionals within the humanitarian sector will add a more nuanced perspective on these crisis situations, especially the cultural, political, and economic implications of humanitarian assistance. Finally, this study will provide an assessment of humanitarian intervention in Lampedusa following unprecedented immigration resulting from the Arab Spring movement. Findings from the study suggest that government involvement, donor influence, and the organization’s motives affect the ability of organizations to effectively provide assistance to vulnerable populations in crisis situations.
Inquiry into the Moral Implications of American Exceptionalism and the U.S. War Ethic

Margaret Thatcher once said that while Europe was created by history, America was created by philosophy. The rudimentary aspects of that philosophy are understood across the United States: students today are taught that, as Americans, they have certain unalienable rights, which include Life, Liberty, and the Pursuit of Happiness. However, our perception of those characteristics which make the U.S. unique - those traits which contribute to our national sense of exceptionalism - conveniently fails to extend to all aspects of our nation's traditions. In particular, the American conception of just war falls outside the bounds of modern just war theory, and has shaped our national identity by influencing not only international political decisions but also our economy, which has been almost since our inception, reliant on the industrial military complex. An inherent respect for natural law has defined the political and defensive infrastructures of the U.S., and contributed to the national divergence regarding the appropriate form for our national security mechanisms. Unlike other nation states, most of which adopted a notion of just war that existed in conjunction with a local religion or established social norm, the United States, born of successful rebellion, has molded its cultural ethos from the clay of its revolution.

In this research I have examined the sources of the U.S.’ national ideology while assessing the complications that resulted from the use of largely untested political doctrines in the New World. More specifically, I have isolated the defense structure of the U.S. for ethical analysis and evaluated the birth of the U.S.’ concept of just war in conjunction with its understanding of unalienable rights and a respect for natural law.
COLUMBIA COLLEGE OF ARTS & SCIENCES


Albeit a few exceptions, scholars of the early Cold War era have ignored the 1960s as a time of gay social activism and community building in Washington, D.C. Those who have conducted research on this subject have analyzed the District through a scope of oppression and persecution, often citing police raids of gay bars and cruising areas as evidence. I, however, think that these raids prove exactly the opposite. In fact, gay men and lesbians, as well as police, saw social venues as important to homosexual identity and culture. These places provided a space for visibility, and were clearly perceived as a threat to "normalcy."

After reviewing newspaper articles, advertisements, and "homophile" publications produced by the Mattachine Society, personal correspondence and legal victories for gay citizens—all prior to the Stonewall Riots, which is commonly cited as the "spark" of the gay rights movement—it has become apparent that a vibrant subcultural nightlife did exist in 1960s Washington. This was, indeed, met by resistance from local authorities; yet, police regulation did not stop a continued presence at "gay" bars, nor did it keep gay men from "cruising" through Lafayette Park.

Specifically, I am looking at any shifts in gay socialization that occurred between the 1960s and 1970s in Washington. I hope to prove that, although 1960s D.C. did offer social barriers for homosexuals, they overcame such restrictions in the public sphere through occupying space, and standing up for their rights, which laid the groundwork for social and political reform, and the creation of new social spaces in the 1970s.
Framed Fright: Literary Techniques Used to Convey a Moral in Jeremias Gotthelf’s “Die schwarze Spinne” (The Black Spider)

Die schwarze Spinne, a novella by Swiss author Jeremias Gotthelf, opens at the festivities for a child’s baptism, during which the farming community is more concerned about appearance, wealth, and status than about piety for the holy rite. In the midst of the celebration, a wise town elder relays a true story from the town’s history, when spiders terrorized the farming community as the result of a pact with the devil. The town was only liberated through brutal suffering and sacrificial death. The seemingly straightforward moral message, that obedience to God and continuous piety are the only means to salvation, is perverted by the way in which it is delivered. In this literary exegesis, I explore the literary techniques of framing and the horror genre and elucidate how they are used to deliver a moral message. The framing technique serves three key functions: to create a context, establish a community, and avert a threat. I examine Gotthelf’s use of the horror genre through Patrick Ludwig’s concept Widernatürlichkeit (perversion of the natural): the extreme, even grotesque corruption of the natural world. I identify Ludwig’s sense of Widernatürlichkeit in the story through horrific events, such as the monstrous, poisonous spider erupting from one character’s face. I propose an expansion of his definition to encompass the less extreme -- but still threatening -- perversion of the norm, represented through foreignness: Characters from outside the community who look and behave differently are indisputably to blame for the horror that the community experiences. My examination elucidates how the fear and coercion created by these literary techniques cause a moral contrast in the novella: instead of a compassionate God, a non-intervening, even absent God is portrayed.
The Americans with Disabilities act was signed into U.S. law in 1990. Yet there is still no comparable law for countries within the European Union regarding accessibility for people with disabilities. An estimated 14 percent of people living in Europe have some form of disability, according to the European Disability Forum. The lack of accessibility in Western Europe ultimately prevented me from studying abroad in Florence, Italy. As a person with cerebral palsy and a wheelchair user, I was firmly discouraged from attending the program I was accepted to because of the lack of accessibility.

This past January, a cameraman and I went on a three-week journey throughout Western Europe to show what accessibility was like in these countries. I interviewed 13 wheelchair users living in five Western European countries about their lives and the accessibility of their communities. We also filmed the difficulties I faced getting around Europe in a power wheelchair. My research about European accessibility will be presented as a documentary film.

While the accessibility in Western Europe is not completely non-existent, I found major holes that do not exist in major U.S. cities for people with disabilities. This included the lack of accessibility to businesses, inaccessible public transportation and unpaved surfaces that made for unpleasant rides for any wheelchair user. In addition to the lack of physical accessibility in some of these countries, several subjects that were interviewed said that they do not feel like first-class citizens, sometimes struggle to find employment and feel socially isolated.
An Unexpected Failure: The Fort Dearborn Project and Urban Renewal in 1950’s Chicago

When the elite, well-funded developers of Chicago’s Fort Dearborn Project announced their multi-million dollar effort to remake a large section of the Near North Side in March 1954, they could not have expected that their bold plans, architectural renderings, and scale models would be worthless in a little over five years. Armed with power and influence backed by an enviable Rolodex of national and local leaders in what was, after all, the era when a transnational network of city planners and developers collectively sought to remake the city, the project nonetheless ended in failure. But what caused this breakdown? Broadly speaking, in tracing the death of urban renewal, historians have pinpointed its demise within a paradigm of inherent inequality and typically racialized prejudices incapacitated by insurgent grassroots community opposition from activists and even insiders, its doom spelled by its essentially undemocratic nature, if not empirical failures discernible to even the casual observer.

Certainly some whose homes or businesses were slated to make way for office towers or high-end residential uses did voice opposition to the project. Yet within the cacophony of opposition, another group—stronger, fueled by self-interest, and also enabled by influence—played a considerable role. My research is situated in the world of 1950’s Chicago businessmen and responds to contemporary reflections by Edward Banfield and Peter Clark, as well as more recent scholarship by Joel Rast, drawing on internal memorandum, correspondence, and other documents to trace the failure of a project that, by all indications, should have succeeded. Conflicting business interests, as well as the perhaps surprisingly ephemeral nature of real estate development within the capitalist and consumerist heyday of the 1950’s are key factors. Further, building upon the work of several generations of urban political theorists, these interactions illuminate important power dynamics within the city.
What Can Last Names Tell Us About Ethnic Inequality in Ecuador?

In the recent Ecuadorian constitutional reform of 2008, the nation acknowledged its diversity and included a focus on decreasing inequality and recognizing Ecuador as a Multicultural and Multinational country. This provides an interesting opportunity and strong need for studies that measure the impact of such policies on ethnic inequality. The lack of research on discrimination and inequality is attributed to a lack of statistical information that takes ethnic minorities into account. Studies also face the challenge of identifying ethnicity and often rely on self-identification and language to indentify indigenous population. In this paper I answer to the need for more research on the chronic issue of inequality with a special focus on ethnic inequality. I pioneer an innovative approach to identify citizens with indigenous last names and whether there is a correlation between having an indigenous last name and income. I use information from the Civil Registry to compile demographic characteristics and data from the Ecuadorian Tax Authority for information on income and industry information. I use ordinary least squares model as a benchmark and conclude with a quantile regression analysis.
Post Arab Spring, Why Monarchies May Not Be the Problem: A Look at Democratization in the Middle East

BACKGROUND/OBJECTIVES
As the Arab Spring moves into the realm of history, certain trends have become clear. What predominates these events is how stalwart monarchies were against the tide of rising social discontent. The goal of this research is to understand why monarchies withstood change better than republics, and analyze the apparent strengths of monarchs to see if they can be manipulated by reformers. Kuwait and Oman were used as case studies.

METHODS
Academics and political activists both inside and outside of Oman were interviewed, in conjunction with off the record conversations and a literary review, to determine how the non-government elite interpreted the events of the Arab Spring. Interviews were recorded, conducted in public coffee houses, and by email and phone when necessitated.

RESULTS
A number of factors help set monarchies, particularly petrodictatorships, apart from the tide of revolution. The key elements are: access to continuous flows of revenue from oil and gas (the rentier theory, contributes to patronage), dependence on the public sector for the majority of national employment and services (related to rentier theory), social contracts that provide tribal and/or religious legitimacy to kings, greater international unity and cooperation (the GCC, peninsula shield in Bahrain for example), and political institutions better designed to be flexible (can co-opt any ideology, can cede legislative powers without losing executive ones).

CONCLUSION
These aspects generate greater stability, and thus make changing the status quo difficult. Nevertheless, with the decline of rent and increased domestic civil society and external pressure, managed reform may now be a pragmatic and realistic solution for both international actors and local citizens.
Plan 3000 is an invasion community on the outskirts of Santa Cruz de la Sierra, Bolivia. Originally a relocation effort for the victims of a grave flood of the River Piraí in 1983, it has grown from 3,000 original families to a large urban community of around 400,000 residents. The poor and indigenous population of the Plan is very oppressed by the country’s powerful conservative elite, whose historical nucleus of power has been Santa Cruz. Using formal and informal interviews with community members and leaders as well as observations, I was able to gain a comprehensive and structural account of a community that lacks written documentation. Using Karl Marx’s Capital and the Communist Manifesto, I argue that the tension in Plan 3000 comes from a Marxist relationship between the bourgeoisie of Santa Cruz and the proletariat of the Plan. The majority of the residents in Plan 3000 lack access to their own means of production, and therefore work directly for the traditional oligarchy. The community has no political rights or basic services such as education and healthcare, and I implement a Marxist analysis to explain the forces impeding socioeconomic development in the community. Currently, the people of Plan 3000 are fighting on many different fronts in hopes of achieving a true social revolution and a chance at true development.
Comparing Approaches of NGOs to Children of Incarcerated Parents in Kathmandu

With the Sigelman Undergraduate Research Experience Award from the Honors Program, I will spend two months this summer living in Kathmandu, Nepal conducting a comparative research study of non-profit organizations in Kathmandu that address the needs of children of incarcerated women, many of whom live in prison with their mothers. By focusing on five organizations with similar program models, I will compare and contrast these approaches while simultaneously analyzing the extent to which these organizations collaborate or compete with each other. This in turn will show how organizational interactions affect the non-profits’ ability to address the needs of children of incarcerated women in Nepal.

I will be living on-site at The Early Childhood Development Center (ECDC), an organization that runs a residential home and kindergarten program for these children. I will take daily Nepali language classes, conduct interviews with program officials and community members, and spend extensive time observing and interacting at these organizations. By spending so much time observing these approaches and learning the complexities of this issue, I hope to come closer to quantifying the number of children who remain living in prisons alongside their incarcerated mothers, which may be as few as 80 children throughout Nepal.

The greater implication of this research will address to the larger question of how non-governmental organizations pool resources and information or communicate to further their shared goals, or how these goals fail to be realized because of competitiveness or other interpersonal problems within and between these organizations. My research will also add knowledge to this under-researched issue and help me pursue further research projects regarding this same phenomenon in Nepal from different angles.
The Straight Path: A Study of Islam and International Politics

Proposals for change or negotiation in Muslim countries that only consider secular factors are too narrow. Proposals should take into account the religious component of Muslim nations. Understanding the way in which religion fits into a country’s perspective, allows greater insight for proposing changes for a lasting compromise. In Arguing Just War in Islam, John Kelsay demonstrates how Just War theory, a western concept, rooted in Catholic theology, could be adopted in Islam, finding support in the Qur’an and other holy texts. The uniqueness of this argument was that he was justifying Just War through Islam, not through Western concepts of democracy or Catholic doctrine. Similarly, in my research I would be considering the international decisions of Turkey, Indonesia, and Iran along with the religious texts that influence Muslim countries. The goal of my project is to understand how Iran, Turkey, and Indonesia- all predominantly Muslim countries- incorporate Islamic beliefs politically when dealing with other countries. I will research each country’s foreign policy by reading books and articles in databases, as well as, interviewing representatives at their respective embassies in Washington D.C. I will compare the ways in which each country incorporates Islam into their foreign policy. Through this process, I also hope to counter the competing understandings of Islam with my own; I hope to gain greater clarity on a religion that has been misunderstood. This broader understanding is key to proposing new ideas for conflict resolution between predominantly Muslim countries and the Western world.
In 1998, Northern Irish civil conflict came to a political end with the Good Friday Agreement. The Agreement brought with it the challenge of realizing this political peace among the greater divided citizenry of Northern Ireland. In efforts to ease this process, Northern Irish Government allocated funds to projects designed to foster development of civic peace. These funds were used for a variety of projects among them several arts, and specifically dance, projects. The object of this study is to analyze if, why, and how one such dance project in Toome, Northern Ireland has or has not been successful in building constructive community relations in a divided post-conflict setting.

Data was gathered through interviews in Northern Ireland with participants of the dance project under study, arts administrators responsible for development of this and similar projects, artists involved in related community-building work, and elected government officials responsible for project funding. Results determined the dance project successful in building constructive community relations in a post-conflict setting. Results identify elements principally responsible for this success as dancing itself, tea ceremonies between dances, allocation of operative responsibility to project participants, and government support for the project. Research is currently being analyzed the impact of additional factors on the project’s success, particularly age of participants and location of project meetings.

Though as a singular case study, these results may not initially appear widely generalizable, data suggest that dance has contributed to a broader community-building effort across Northern Ireland through a network of similar dance projects. Further analysis of data and conceivably additional research concerning this network are necessary to determine the significance of this phenomenon. The research consequently provides a strong introduction to understanding dance’s potential as a post-conflict reconciliation tool and invites further research to better understand its relevance in mediating contemporary sectarian divides.
In the wake of globalization and demographic shifts, the concept of security is evolving because it is no longer synonymous with military issues and defense. Today, the understanding of security has developed to include protection of communities from internal threats. This definition is a result of the rapid change of current times. Environments are continuously changing for humans, and infectious disease stands as an important security threat. Infectious disease can travel across borders, affect populations regardless of wealth, and break down societies with the resulting morbidity and mortality. It kills more than eleven million people a year, causes 63 percent of all childhood deaths and 48 percent of premature deaths on a global scale.

Through my research, I analyze the threat infectious disease imposes on global security. I identify the global spread of infectious disease through migration, natural disasters, humanitarian emergencies, and emerging and re-emerging infectious diseases. I evaluate approaches of the World Health Organization, the International Organization for Migration, and specified individual actors to reduce infectious disease spread. In addition, I illuminate the understanding of the relationship between infectious diseases and security as understood by global health and security experts.

I conclude that infectious disease is a major threat to global security. However, it is not the primary security concern in many states since it is not well understood as a direct threat to security by the traditional security community. Additionally, it is difficult to measure the success of fighting infectious disease expansion with prevention efforts. In order to raise health on the security agenda, international organizations and governments of developed countries need to build capacities and capabilities in those less developed as well as spread awareness about the true dangers of infectious disease, especially with increased movements of people.
Almost immediately following the overthrow of Saddam Hussein’s regime in 2003, the war in Iraq became characterized by the fight against insurgents. A key aspect of Counterinsurgency (COIN) is building trusted networks -- put simply, “winning hearts and minds.” Monetary compensation is considered a means to this end. This paper evaluates the US Military’s use of condolence payments in Iraq, which compensate Iraqi civilians for death, injury, or property damage caused by American forces. Through analysis of records released under the Freedom of Information Act and interviews of military officials with experience adjudicating claims and payments, this research determines that there are several factors that limit the effectiveness of current policy. First, the Foreign Claims Act, one of the main ways through which the US makes payments, is hindered by its “combat-exclusion” restriction. Second, although individual commanders can circumvent this restriction by using other funds, this alternative method of providing condolence payments is not institutionalized. This informality causes compensation to be given inconsistently, which has the potential to further alienate the population and prove counter-productive. These conclusions necessitate further study, but the US military has not released most of the data it collected on claims and payments in Iraq. Nevertheless, this qualitative analysis has clear implications for COIN efforts and provides an important piece of situational awareness for both uniformed and civilian leaders.
Jurassic Dinosaurs from the Gobi Desert of Northwestern China

A series of joint expeditions by GW and Chinese Academy of Sciences researchers and students to the Shishugou Formation in the western Gobi Desert of Xinjiang, China, has amassed one of the most extensive collections of dinosaurs and other terrestrial vertebrates from the late Middle-early Late Jurassic. Among the most significant finds are one of the oldest tyrannosaurid dinosaurs (Guanlong wucai, Nature 439:715-718), the oldest horned dinosaur (Yinlong downsi, Proc. Royal Soc. London B 273(1598):2135-2140), a toothless theropod dinosaur with important implications for the origin of the hand of birds (Limusaurus inextricabilis, Nature 459: 940-944), and the oldest member of the bizarre theropod group Alvarezsauridae (Haplocheirus sollers, Science 327: 571-574). Limusaurus, Guanlong and several other species were preserved stacked upon each other where they had been trapped in sticky mud, a rare occurrence in dinosaur deposits. Ongoing research investigates the evolutionary relationships of the individual faunal elements and the implications of the fauna for the regional development of endemic faunas as the single supercontinent of Pangaea broke apart.
Mandibular premolar morphology is correlated with dietary toughness in sympatric callitrichids

It has been suggested that mandibular premolar molarization in fossil hominins is an adaptation for the consumption of mechanically challenging food items. This study used an extant primate model to test the hypothesis that premolar molarization correlates with dietary toughness. The callitrichids Callimico goeldii, Saguinus fuscicollis, and Saguinus labiatus are closely related and live sympatrically in the Amazon. Although there is significant overlap in the dietary items they consume, their mandibular postcanine morphology differs. Standard metric and 2D geometric morphometric analyses conducted on the mandibular postcanines of these taxa in the collection of the NMNH demonstrate that, even when the effects of differences in body size are taken into account, Callimico goeldii and S. labiatus have molarized P4s when compared to S. fuscicollis. Food items from the diets of these taxa were collected over a six-week period during the months of June and July 2011 at Camp Callimico, Bolivia and toughness properties were tested using a Lucas field mechanical tester. Among four major food categories (arthropods, exudates, fruits, fungus) masticated by the callitrichid taxa, fungus was found to be significantly tougher than other food items. Fungus accounts for almost one-third the diet of Callimico goeldii, and S. labiatus is known to consume fungus more often than S. fuscicollis, although it does not form a significant part of its diet. In callitrichids, molarized P4s may be an adaptation that allows taxa to shift to a diet with a higher percentage of tough food items.

This study was funded by a NSF-GRFP and NSF-IGERT DGE-0801634.
Longitudinal Weight Calibration in Recurring Large-Scale Sample Surveys

The National Science Foundation’s Survey of Doctorate Recipients is conducted every two or three years and collects detailed information on thousands of individuals receiving PhDs in science and engineering in the U.S. and some others with PhDs from abroad in these areas. Survey weights adjust for oversampling of select groups and nonresponse on a cross sectional basis. A significant portion of the sample (e.g., 60% on 3 or more surveys from 1993-2006) appears in multiple survey years and can be linked across time. No longitudinal weight exists that would enable estimation of statistical models or comparison of finite population characteristics using data from multiple survey waves together. This poster presents idea of survey weight calibration for the purposes of enabling longitudinal analysis using multiple survey waves. Methods presented here have potential applications in several large-scale federal surveys. The poster reviews the practice of survey weight calibration, explains the proposed method, and demonstrates results. Research topics for dissertation development, including producing positive weights, variance estimation, and the use of multivariate calibration targets are highlighted.
Landscape Neotaphonomy and East African Carnivore Guild Structure: Modeling Hominin Scavenging Opportunities

Landscape-scale bone assemblage structure and the amount of carcass resources available for hominin consumption are determined in part by population densities of carnivores relative to those of their prey and by carnivore guild structure. Because of hyenid bone-cracking adaptations, their population density compared to that of other carnivores such as meat-slicing large felids has a significant impact on what animal resources remain on the landscape after the initial predation event. Based on observations in Serengeti National Park/Ngorongoro Conservation Area (Tanzania) ecosystem, it is argued that among different habitats, those with large numbers of hyenas, particularly spotted hyenas (Crocuta crocuta), will present fewer scavenging opportunities for hominins. Neotaphonomic surveys in Amboseli National Park (Kenya) ecosystem document the effects of changing spotted hyena densities over time on bone survival and carcass fragmentation. In this study, we compare data on carcass fragmentation and bone destruction from Serengeti/Ngorongoro study with long-term data from Amboseli and new data from Shompole Conservation Area in southern Kenya. We test the generality of the relationship between spotted hyena density and carcass fragmentation across different habitats and through time. In environments with the highest spotted hyena density, we find the lowest skeletal element evenness (an index of carcass completeness), depressed axial skeletal element frequencies, and increased deletion of long bone epiphyses. Based on our observations in modern ecosystems, it is clear that past hominin scavenging opportunities must be considered in the context of dynamic ecosystems in which the abundance of bone-cracking carnivores can change over time and across habitat boundaries. Past scavenging opportunities would be expected to increase in times and places where bone-cracking members of the carnivore guild were relatively rare, suggesting that the abundance and paleolandscape distribution patterns of associated stone artifacts and hominin-modified vertebrate remains could reflect varying Plio-Pleistocene carnivore guild structures.
Subcellular Analysis by Laser Ablation Electrospray Ionization Mass Spectrometry

Heterogeneous distributions of metabolites in subcellular domains stem from local reactions and transport processes that in turn can be affected by molecular crowding. Although certain metabolite distributions can be followed by secondary ion mass spectrometry or fluorescence microscopy, most methods for the subcellular analysis of eukaryotic cells rely on the isolation of organelles by fractionation techniques based on cell disruption and differential centrifugation. Such sampling-related perturbations likely alter the metabolite concentrations within a cell. Recent advances in mass spectrometry have led to the metabolic analysis of single cells and have provided insight into cellular heterogeneity. Laser ablation electrospray ionization (LAESI) mass spectrometry has been utilized to directly study single cells in the ambient environment. By combining cell microdissection with LAESI mass spectrometry, we are able to perform in-situ subcellular analysis of metabolites at atmospheric pressure. In these experiments, the cell membrane of an Allium Cepa epidermal cell is cut and peeled back with a tungsten microdissection needle to expose the subcellular components. An etched optical fiber is used to deliver mid-infrared laser pulses to the subcellular region of interest. The ablation plume containing sample related particles is ionized by an electrospray plume and analyzed by a mass spectrometer. Over 30 ions are detected from a single cell nucleus, and over half of them have been tentatively assigned to primary metabolites including amino acids and carbohydrates. Large differences are observed in the abundance of certain metabolites between the nucleus and cytoplasm and multivariate statistical methods point to metabolites that are primarily localized in either the cytoplasm or the nucleus. Local production or consumption of metabolites, or the presence of an active transport mechanism, may contribute to these large concentration gradients.
A Cytoscape visualization method contrasting the all-against-all proteome correlation matrix versus the classic taxonomy tree.

**Background**

The classical approach to naming and classifying biological organisms primarily relies on grouping organisms according to similar physical and behavioral attributes. The resulting taxonomy tree may not accurately reflect ancestry as reflected by advances in genome sequencing. An effort headed by the Protein Information Resource (PIR) has computed all-against-all correlation values between all complete proteomes and made this data available for public use. I have developed a Cytoscape method to visually illustrate genomic similarity between proteomes using the NCBI taxonomy tree and PIR correlation matrix.

**Findings**

Using Cytoscape version 2.8.1 network visualization software, data files containing the NCBI taxonomy tree, the PIR complete proteome correlation values matrix, and other auxiliary files were imported to produce a novel modified taxonomy tree graph of proteomes according to their genomic similarity. The results were validated against the PIR representative proteome data set to identify species that are distantly related per the taxonomy tree but have high sequence similarity. The NCBI taxonomy tree suggested that the fungus Aspergillus niger CBS 513.88 (ASPNC) is a descendent of Aspergillus niger (ASPNG). However, from the taxonomy-correlation graph was clearly seen that ASPNC should meet ASPNG at a higher taxonomic rank since the graph positioned ASPNC closer to other children of Aspergillus, such as Aspergillus flavus. This was confirmed with a similarity score difference of 0.13% for Aspergillus niger to ~34% for the Aspergillus flavus and Aspergillus oryzae families.

**Conclusion**

This method is suitable for illustrating the differences between the NCBI taxonomy tree classification and the PIR representative proteome group classification. Proteomes with high genomic similarity will be clustered together and be easily traceable back to their parent taxa. Potential applications include protein classification and characterization. Efforts are underway to make interactive pre-generated graphs web accessible.
Achieving efficiency and accuracy during Oldowan stone tool production

It is now clear that multiple hominin species used and/or produced stone tools, yet evidence suggests that only later Homo intensified and developed the behavior. This difference has been attributed to later Homo’s ability to execute efficient tool production, to the exclusion of earlier hominin species. The current study evaluates whether modern human upper limb anatomy contributes to energetic efficiency and/or accuracy during knapping. Knapping kinematics were captured from eight experienced knappers using a VICON motion analysis system (200Hz). Each subject produced four Oldowan choppers under two conditions: two choppers under normal conditions and two with subjects’ wrists restrained to ~30° of extension to simulate one aspect of the primitive hominin condition. Under normal conditions all subjects employed a partial proximal-to-distal joint sequence, with peak segment linear velocities and peak joint angular velocities initiating at the shoulder and elbow, respectively, and progressing distally. Subjects exhibited the “dart-throwers arc,” moving from wrist extension/radial deviation to flexion/ulnar deviation. Wrist extension peaked 0.037-0.075 seconds before strike, positioning the wrist to reach peak flexion velocity immediately before strike, resulting in peak hammerstone acceleration at strike. Preliminary results suggest that together these motions patterns produced significantly more work in an energetically efficient manner compared to swings when the wrist was restrained and precluded from being positioned for rapid flexion. Further, with an unrestrained wrist subjects struck their targets with significantly greater accuracy (p < 0.05). These results suggest that derived hominin hand and wrist anatomy contributes energetic efficiency and accuracy to stone tool production.
Realizing Groups as Distributive Sets

A binary operation is a way to associate an element of some set to each pair of elements in that set. For instance, the associations of “the closest descendant to” and “the closest common acquaintance of” two people is a binary operation on the set of all people (alive or dead). Distributivity is a relation between two binary operations that restricts the way they are composed. In the case above, it amounts to the statement “the closest descendant of Chris and the closest acquaintance of Alice and Bob is the closest acquaintance of the closest descendant of Alice and Chris and the closest descendant of Bill and Chris”. If this statement is true for all trios of a particular set of people, then the associations of “closest descendant” and “closest acquaintance” are said to distribute. In this paper, we show that any example of a certain type of mathematical object called a “group” may be embedded into a distributive set.
Reconstruction of Paleo-Permafrost Environments in the Mid-Atlantic Region

Compared to Russian and other European work, relatively little research has been done in North America on past-cryogenic (cold climate) weathering and relict permafrost-related features. However, during the last decade, relict periglacial structures and sediments have been identified along the Mid-Atlantic Coastal Plain. This work evaluates the paleo-permafrost environments in the Mid-Atlantic region during the Pleistocene, including the last glacial maximum. To investigate extent of paleo-permafrost, periglacial features were investigated and soil samples were collected at several locations representing a north-south transect in Delmarva region. Samples were analyzed using a mineralogical analysis called the Coefficient of Cryogenic Contrast (CCC). The CCC is based on a ratio of quartz to feldspar in different fractions and is indicative of cryogenic weathering. To establish a baseline for past cryogenic conditions, an additional set of soil samples was taken from a contemporary permafrost environment in Alaskan Arctic. CCC values obtained from both transects will be used as proxies for the Mid-Atlantic ground temperature regimes during the late Pleistocene. While CCC analysis of Mid-Atlantic samples is underway, the results from the Alaskan transect are indicative of contemporary conditions of cryogenic weathering and can be used to establish a relationship between paleo-permafrost extent in Mid-Atlantic Region and contemporary permafrost extent in Alaska. The established relationships will be used to evaluate the geography and extent of the periglacial environment during the Pleistocene and will help in better understanding of the evolution of the environment and climate in Mid-Atlantic region.
Homology of a Small Category with Functor Coefficients and Barycentric Subdivision

In Economics, e.g. Game Theory, barycentric subdivision of a simplicial complex is a powerful tool used to study the Nash Equilibrium. It is well known in classical algebraic topology that homology of a simplicial complex is preserved by barycentric subdivision. We introduce the definition of homology of a small category with functor coefficients and generalize the result that homology of a small category of an abstract simplicial complex is not changed by barycentric subdivision.
Single Cell Analysis of Saccharomyces cerevisiae on Silicon Nanopost Arrays by Laser Desorption Ionization Mass Spectrometry

A single Saccharomyces cerevisiae (yeast) cell represents a minute amount of sample, a mere 30 femtoliters in volume. Comprehensive analysis of such limited amounts of material is a major challenge that requires a combination of highly efficient ion production and mass spectrometry. Photonic ion sources rely on specially designed nanostructures that efficiently harvest energy upon laser excitation, resulting in dramatically enhanced ion yields. Laser desorption ionization (LDI) from silicon nanopost arrays (NAPA) has been shown to provide ultra-low limits of detection (~800 zeptomoles) and a wide dynamic range for the direct analysis of untreated complex mixtures, such as intracellular metabolites from microorganisms. Understanding the metabolic processes in microorganisms, e.g., S. cerevisiae can reveal how biological systems grow, develop, and interact with the environment. In this study, NAPA chips have been used for the analysis of intracellular metabolites in small populations and single cells of yeast. Using 79 yeast cells we have successfully detected 17% of the metabolites in the known yeast metabolome (109 of 657 metabolites) and achieved a 67% coverage of the 94 most significant pathways. When reducing the number of analyzed cells to a single cell, up to 4% of the known metabolites, belonging to 29% of the major biochemical pathways, were still assigned. Importantly, the ion intensities for the various metabolites appeared to reflect their quantities in the cells between cell counts of 1 and ~80. To gauge the metabolic response to stress, the effect of oxidative environment on the metabolome of yeast cells was explored. Our results indicated that metabolic changes within small cell populations could be accurately captured using NAPA and LDI. This approach and the related findings can be used to test metabolic network models and to enhance systems biology studies on cellular heterogeneity and response, and ultimately improve the understanding of microorganisms.
Anti-bacterial activity of a recombinant Sp185/333 protein from the California purple sea urchin, Strongylocentrus purpuratus

The California purple sea urchin possesses a sophisticated innate immune system that functions without adaptive immune capabilities. It responds to pathogens effectively by expressing a highly diverse array of Sp185/333 proteins. The deduced sequence diversity of Sp185/333 proteins suggest that they are involved in immune responses against pathogens. Individual sea urchins can express more than 260 distinct Sp185/333 proteins. One speculation on the level of diversity of the Sp185/333 proteins is that different versions may have different immune functions. Although the deduced proteins display striking diversity, they share an overall organization and structure with a hydrophobic leader, a glycine-rich N-terminal region with a RGD motif (integrin binding), a histidine-rich region, and a C-terminal region. There is no transmembrane region and no cysteines in the deduced sequences. The amino acid composition suggests that the proteins are intrinsically disordered and thus it is impossible to predict secondary and folding. The lack of homology with known proteins precludes any functional predictions, but the conserved leader and RGD motif provides clues that these proteins may be secreted and interact with cell surface integrins. Furthermore, the partial positive charges in the histidine patches make the Sp185/333 proteins attractive candidates for immune effectors that include bacterial binding. With the aim of identifying the Sp185/333 protein functions, we produced a single recombinant protein (rSp0032) and evaluated its function using flow cytometry in a series of bacteria-protein binding experiments, competition and displacement assays. Results strongly suggested that rSp0032 is capable of specific, non-reversible and stable binding against marine Gram negative bacteria, Vibrio diazotrophicus. This has laid the groundwork for future studies to evaluate the rSp0032 mechanism of action.
Is Lac Anony Reaching its Tipping Point?
A Comparative Case Study of the Traditional Fishery at the Village of Antsovela

Lac Anony, the largest brackish body of water in the south of Madagascar, maintains a dynamic relationship with the Indian Ocean, mixing fresh and saltwater. The periodic opening and closing of the lake basin to the ocean allows for a unique fishing environment that the surrounding local villagers have used for decades as their primary livelihood. The current barrier between the lake and the ocean has lead to a decline in aquatic resources, greatly affecting the lives of the locals. As human population in the region increases and climate changes, concern over the potential destruction of the Lac Anony fishery has arisen. In this study, a two-week immersion in the village of Antsovela, personal interviews with the local villagers, surveys of fish caught over the course of ten days in Lac Anony and surveys of vendors selling fish in a nearby market are conducted in order to gain an understanding of the current state of the fishery. This data is compared to that of Pierre Lamarque’s study of the fishery of Lac Anony, and specifically of the village of Antsovela, conducted in 1953 in order to gain an understanding of the progression of the traditional fishing industry over the course of 58 years. The results reveal a large increase in population, change in the type and abundance of species caught in the lake, little change in the methods used by fishermen and weak regulations on the traditional fishing industry. Therefore, management and development of the fishery is necessary for its continued survival. Collaboration between international aid, the Malagasy government, and the local villagers is imperative for the sustainability of rural livelihoods and the aquatic environment.
Combinatorial approach to some Heegaard Floer homology theories via branched spines

BACKGROUND
Heegaard Floer homology theories are a powerful tool for the classification of 3-manifolds. However, the constructions involved are often prohibitively complicated. The two main constructions we focus on are those of Sarkar–Wang and Ozsvath–Stipsicz–Szabo for combinatorial descriptions of \( \widehat{HF} \) over \( \mathbb{Z}_2 \).

METHODS
Regarding the above constructions, we show how branched spines lead to a natural presentation of 3-manifolds which encodes much of the necessary combinatorial data (possibly even over \( \mathbb{Z} \)) in a convenient manner. We hope that by comparing the two constructions above with the natural construction from branched spines, a simpler yet more powerful combinatorial description may be found.

RESULTS
We have shown that for \( S^3 \), when calculating \( \widehat{HF} \) over \( \mathbb{Z}_2 \) our construction leads to a complex with only 8 generators and 12 differentials, compared to 80 generators and 150 differentials for Sarkar–Wang and well over 1000 of each for Ozsvath–Stipsicz–Szabo.

CONCLUSIONS
Using branched spines to approach Heegaard Floer homology theories greatly reduces the complexity in some cases.
Finding Finite Topological Spaces

We are interested in studying finite topological spaces using computers. It is therefore useful to construct a list or database of such spaces. However, it is a non-trivial problem to efficiently see when two spaces are homotopic or even homeomorphic. Two spaces are homotopic iff they have the same irreducible core. Thus we only include in our list spaces that are irreducible cores, i.e., spaces which do not admit any deformation retraction.
Visible light extinction was measured at a height of 20 mm above the fuel tube exit in a nitrogen-diluted, ethylene/air, non-premixed flame and this data was used to determine the optical band gap, $E_{\text{opt}}$, as a function of radial position in the flame. This height was chosen as previous measurements in our laboratory have shown substantial Raman scattering from thermophoretically-sampled, carbonaceous material at this flame location. Further, this height is at the onset of large signal intensity in annular flame regions from laser-induced incandescence measurements. In our previous work, analysis of the Raman spectrum suggested the source of the scattering was PAH species with sp2 conjugation lengths of 1.0 – 1.2 nm, consistent with a molecular mass range of 500 -1000 Da. In the current work, a super continuum light source will be spatially filtered and then focused into the flame. Transmitted light will be recollimated and then directed into a spectrometer. After tomographic reconstruction of the radial extinction field, the optical band gap will be derived from the near edge absorption spectrum using a Tauc analysis. This method is the same approach taken in work last summer, which used a light emitting diode, with center emission wavelength of 445 nm, as a light source. The results from that work showed an optical band gap of, $2.38 \pm 0.08$ eV, which was compared to calculations of the electronic structure of a series of D2h polynuclear aromatic hydrocarbon (PAH) using time-dependent density functional theory. From this correlation, the measured band gap suggested that the source of the extinction could be a PAH with as few as 10 aromatic rings. The supercontinuum source provides better spectral resolution, more intensity, and an extended spectral coverage for these measurements.
Low cost laser heterodyne radiometer for highly sensitive detection of greenhouse gases

Laser heterodyne radiometry (LHR) is a spectroscopic technique that allows for the detection of a weak signal via technology that is adapted from radio receivers, wherein a weak input signal is mixed with a stronger local oscillator and the difference between the two frequencies (the intermediate frequency or beat frequency) carries the information of interest. In the case of LHR, the weak signal is light that undergoes absorption from trace gases in the atmosphere and the local oscillator is a laser tuned to a frequency close by. Preliminary efforts to observe a heterodyne beat in a laboratory setting is in progress, with the end goal of working in conjunction with NASA Goddard to produce a prototype field instrument capable of measuring absorption of the significant carbon cycle gases in the atmospheric column, carbon dioxide (CO2) and methane (CH4), along with molecular oxygen (O2) in order to establish atmospheric pressure. The use of distributed feedback (DFB) telecommunications lasers are desirable for use as local oscillators as they are not only cost-effective but they are commercially available in frequencies that can be tuned to specific features in the rotational spectra of the gases of interest. In the current setup, the beam from a DFB laser tuned to 1532.27 nm is split 50/50 via a 2 x 2 single mode fiber splitter. One beam passes through a standard HCN cell while the other beam is directed through an acousto-optical modulator (AOM) which shifts the frequency of the beam by 80 MHz. The HCN cell was chosen because there is a feature in the absorption spectrum of HCN centered at approximately 1532.28 nm. The two beams then get coupled back onto single mode fiber, where they are mixed on a fast photo receiver and the spectrum is analyzed with an RF analyzer.
Distributive Subgroups Inside the Monoid of Magmas

Let X be a set and Bin(X) be the set of magmas (binary operations) on X. We endow the set Bin(X) with a monoidal structure by defining the composition of two binary operations and then noting the existence of an identity. Within this monoid we hone in on distributive sets (subsets of Bin(X) whose elements are all mutually right-distributive). In particular, we look for distributive sets which form groups, an important mathematical object which captures the notion of symmetry. By using computational and algebraic techniques we have identified the dihedral group (the symmetries of a regular polygon), and we consider extensions of these techniques to identify other finite groups in Bin(X). In addition, we use a computer to fully classify all distributive groups contained in Bin(X) for |X| <= 6.
Investigating the roles of mRNA in early Xenopus embryo development

As the development of an embryo proceeds, its cells become committed to specific fates and their developmental potentials are gradually limited. A cell’s fate and potential is influenced by a variety of factors. Results from previous research suggest that transcription factors, proteins that activate the expression of specific genes, play a major role in dictating developmental stages and cell fate. This project examines when and where some of these transcription factors act and what causes their expression in Xenopus (South African clawed frog) embryos. In vitro transcribed mRNAs coding for the transcription factors gem, zic2, sox11, and foxD5 are injected into specific parts of the embryos along with a lineage tracer, beta-galactosidase. Then, the injected blastomeres are dissected from the remaining cells of the embryos and cultured in simple salt medium until the embryo has developed enough to have an intact nervous system. These explants test whether the expression of the injected transcription factors repress, stimulate, or maintain the expression of neural specific transcription factors (zic1 and sox2) without interaction from other parts of the embryo. The expression of zic1 and sox2 is detected by in-situ hybridization using anti-sense RNA probes. The expression of these two neural genes in control and injected embryos is compared to make conclusions about the roles those injected mRNAs play in neural development. Results to date indicate that zic2 induces the expression of sox2 and zic1, whereas sox11 does not. Blastomere explants injected with gem and foxD5 are being created. This information will be important to understand how neural stem cells are created in the embryo, and be useful for experimental creation of neural stem cells.
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Quantify Ion-modulated Forces between Nucleosomes

Nucleosome-nucleosome interactions play fundamental roles in chromatin assembly and chromosome conformation, and consequently regulate gene expression. The interaction between nucleosomes is in turn modulated by wide varieties of solvent and molecular factors such as ions, post-translational modifications, and histone variants. Here we combine small angle x-ray scattering and theoretical modeling to quantify inter-nucleosome forces in solution as a function of mono- and di-valent cation concentrations. Both natural-source and recombinant mononucleosomes are studied, as well as tail-deletion mutants of interest. Inter-nucleosome forces are found to be much smaller than predicted from the bare or effective charges. Tail-deletion mutations show trends as expected from their roles in mediating inter-nucleosome interactions. We discuss our results on the basis of theories of polyelectrolytes, and attribute the quantitative differences to the non-uniform charge patterns and conformational plasticities of nucleosomes.
The California purple sea urchin possesses a sophisticated innate immune system that functions without adaptive immune capabilities. It responds to pathogens effectively by expressing a highly diverse array of Sp185/333 proteins. The deduced sequence diversity of Sp185/333 proteins suggests that they are involved in immune responses against pathogens. Individual sea urchins can express more than 260 distinct Sp185/333 proteins and one speculation on the advantages of this level of diversity of the Sp185/333 proteins is that different versions may have different immune functions. Although the deduced proteins display striking diversity, they share an overall organization and structure with a hydrophobic leader, a glycine-rich N-terminal region with a RGD motif (integrin binding), a histidine-rich region, and a C terminal region. There is no transmembrane region and no cysteines in the deduced sequences. The amino acid composition suggests that the proteins are intrinsically disordered and thus it is impossible to predict secondary and folding. The lack of homology with known proteins precludes any functional predictions, but the conserved leader and RGD motif provides clues that these proteins may be secreted and interact with cell surface integrins. Furthermore, the partial positive charges in the histidine patches make the Sp185/333 proteins attractive candidates for immune effectors that include bacterial binding. With the aim of identifying the Sp185/333 protein functions, we produced a single recombinant protein (rSp0032) and evaluated its function using a series of binding and competition experiments evaluated by flow cytometry. Results strongly suggested that rSp0032 is capable of specific, non-reversible and stable binding against the marine Gram negative bacterial species, Vibrio diazotrophicus but does not bind Gram positive bacteria. The binding capability indicates that rSp0032 may initiate effector mechanisms to clear an infection. This has laid the groundwork for future studies to evaluate the rSp0032 mechanism of action.
Kepler is a NASA satellite currently orbiting the earth and continuously monitoring hundreds of thousands of stars in its field of view. It does this by taking successive pictures of the sky, which scientists can analyze for changes in the intensity of light for each star system. A change in light intensity can be caused by a change in the star's output of light, by another object passing in front of it, or by a combination of both. At GW, we are currently analyzing a number of these stars. In particular, we are interested in binary star systems called cataclysmic variables (CVs), in which two stars are so close together that they only take a few hours to complete an orbit. By comparison, the Earth takes 365 days to complete its orbit around the Sun. CVs are especially interesting to study because they are among the few stellar systems that change dramatically within a human lifetime. The systems under investigation at GW change dramatically inside a single month. Our analysis indicates that one of the systems under study has an orbital period of approximately 120 min, while another is only 100 min. The detected light output not only shows bursts of radiation, it also includes episodes of even greater output, which we refer to as super outbursts, and associate with an independent orbital period. The underlying causes of these different periodicities are not fully understood but are thought to involve the turbulent transfer of matter from one partner to the other and the possible development of an accretion disk.
Investigating the role of bacterial endosymbionts in insect host immune responses to entomopathogenic nematodes and their mutualistic bacteria

BACKGROUND

Spiroplasma poulsonii and Wolbachia pipiens are bacterial endosymbionts living in Drosophila flies. Survival of endosymbionts in insects requires not only evasion of host immunity, but also that they cause no detrimental effects on host fitness. Drosophila has been established as an excellent genetic model to study the mechanistic basis of the innate immune response to pathogenic microbial infections. The entomopathogenic (or insect pathogenic) nematodes Heterorhabditis bacteriophora are parasitic worms that form a mutualistic relationship with the Gram-negative bacteria Photorhabdus luminescens. The nematode-bacterium complex is able to invade, infect and kill insects. The aim of this project is to investigate the effect of Drosophila endosymbionts on the insect immune response to the nematodes and their mutualistic bacteria.

METHODS

We used Drosophila adult flies carrying Spiroplasma endosymbionts only, Wolbachia endosymbionts only, both Wolbachia and Spiroplasma, and no endosymbionts. These four fly strains were infected with Heterorhabditis nematodes with (symbiotic worms) or without (axenic worms) their Photorhabdus mutualistic bacteria. The mode of bacterial infection involved direct injection into the hemocoel of adult flies using a microinjector. Methods of Drosophila infection with Heterorhabditis involved direct contact of the nematodes with adult flies. Survival results were estimated daily.

RESULTS

Survival data show that Drosophila adult flies carrying Spiroplasma endosymbionts only are more resistant to infections by Photorhabdus bacteria alone, axenic Heterorhabditis and symbiotic Heterorhabditis (nematodes carrying Photorhabdus) compared to flies carrying Wolbachia, both Spiroplasma and Wolbachia or no endosymbionts.

CONCLUSION

Our results suggest that Spiroplasma bacteria living in Drosophila adult flies have the capacity to alter the survival of their hosts upon infection with entomopathogenic nematodes carrying or lacking their symbiotic Photorhabdus bacteria. I am currently investigating whether the presence of endosymbionts in flies affects the total number of hemocytes (equivalent to mammalian white blood cells) in the context of experimental infection with the nematodes and their bacteria. This research will potentially benefit similar immunity studies, not only in other model insects, but also in insects of agricultural or medical importance, like aphids and mosquitoes. It will also contribute to the identification of host immune mechanisms to parasitic infections. Further, it may provide important information on the roles of endosymbionts in conserved immune functions of vertebrate animals. Finally this research may uncover novel nematode or bacterial infection strategies for evading the insect immune system by targeting and destroying host endosymbionts.
Propranolol has been used clinically to reduce myocardial reinfarction rates and sudden cardiac death. Previous studies have shown that treatment with propranolol reduces lipid peroxidation (Mak and Weglicki, 2004). Upon ingestion, the majority of propranolol is metabolized with 4-hydroxypropranolol being a major metabolite. After finding that 4-hydroxypropranolol was more potent and had enhanced antioxidant abilities when compared to propranolol, Mak and Weglicki (2004) proposed that the benefits of propranolol therapy may be due to this metabolite. Based on the structural properties of 4-hydroxypropranolol that make it unique from and a more potent antioxidant than propranolol, this current study aims to further understand the structural factors that are related to the potency of this class of antioxidant compounds. This study is carried out through the synthesis and isolation of stable compounds that are structurally similar to 4-hydroxypropranolol, followed by a TBARS (thiobarbituric acid reactive substances) assay to test each compound’s antioxidant ability. Several of the compounds have been synthesized and isolated and the conditions for the TBARS assay have been finalized. A preliminary analysis of results from the TBARS assay has shown that two-ring compounds have more potent antioxidant properties than one-ring compounds. Currently, final synthesis of two and three-ring compounds and the testing of the synthesized compounds is in progress.
Computability theory, the mathematical theory of algorithms, is the foundation of theoretical computer science. Its goal is to understand the power and limitations of the ability of computer programs, or, more correctly, algorithms. Since the goal is to understand inherent limitations, not limitations due to some particular piece of hardware, the approach is very general and abstract. The most fundamental concept in computability theory is that of a computable relation. A relation is computable if there is a decision procedure for determining in finitely many steps whether given elements belong to that relation. Computable relations describe the so-called decidable problems, ones for which there exist algorithms requiring no external knowledge to compute the result. The undecidable relations are further classified into an infinite hierarchy, based on the amount of the external knowledge needed to perform the computation. This level of external knowledge is called the Turing degree.

My current focus is to investigate computability theoretic properties of orders on computable algebraic structures, in particular computable groups, and how they relate to the topological properties of such orders. A group is computable if its domain is a computable set and its group operation is computable. Orders on groups are special binary relations. More precisely, a left order of a group is a strict linear ordering of its domain, which is left-invariant with respect to the group operation. If the order is also right-invariant, then it is called a bi-order. There is a natural topology on the set of all left orders, and this space is compact even for an arbitrary (not necessarily even associative) structure with a single binary relation. A computable orderable group does not necessarily have a computable order. For familiar computable orderable groups, both commutative and non-commutative, we investigate Turing degrees of their orders.
Diversity of Immune Response Proteins: Sp185/333 Proteins in the Purple Sea Urchin

In defense against pathogens, hosts must generate diverse immune receptors to detect the widest possible range of pathogens and to induce the production of immune effector proteins. Sea urchins lack an adaptive immune system (no lymphocytes, no antibodies), and may have different mechanisms to diversify their anti-pathogen proteins. The California purple sea urchin has about 50 members of the Sp185/333 gene family that encodes a highly diversified repertoire of immune response proteins that are produced following bacterial infection. Over 260 different versions of the Sp185/333 proteins may be present in a single sea urchin, based on differences in size and charge, plus variations in presence and amount depending on the animal and type of immune challenge. Native Sp185/333 proteins can be isolated by affinity to metal ions because of their multiple histidines, resulting in 1-4 bands of unique molecular weight that vary among sea urchins. Although currently underway, we are conducting 2-dimensional gel electrophoresis (which separates proteins by charge and then by size) on nickel-isolated protein samples, followed by Western blot analysis. We will report whether these bands are composed of single proteins or are actually a complex of several variants that have the same molecular weight but differ in charge. We will also address whether the diversity of the nickel-isolated proteins vary among individual sea urchins. Results will broaden our understanding of innate immune diversification in animals such as sea urchins that survive on innate immunity in the absence of antibodies.
Metabolic Analysis of Single Pancreatic Beta-Cells by Laser Desorption Ionization Mass Spectrometry on Silicon Nanopost Arrays

Typical metabolic analysis requires a substantial population of $n > 10^6$ cells, and demand extensive sample preparation. When utilizing a population of this size, metabolic differences between subpopulations are averaged out and their distinction is obscured. The metabolic analysis of single animal cells and small cell populations ($10 < n < 25$) is critical for the exploration of cellular heterogeneity in biochemical processes, such as hormone regulation, environmental response, cell differentiation, etc. The metabolic analysis of pancreatic beta cells is particularly important, as their malfunctioning plays an intrinsic role in the disease diabetes mellitus. Silicon nanopost arrays (NAPA) were recently introduced as a photonic ion source for mass spectrometry. NAPA have exhibited detection limits of a few hundred zeptomoles and a wide dynamic range (up to 4 orders of magnitude).

In a small beta cell population ($n = 25$), we observe ~100 metabolite ions in the laser desorption ionization (LDI) mass spectra from NAPA. About 30 of those ions have been tentatively assigned to primary metabolites such as spermidine, threonine, and uracil. Our preliminary results suggest that we are able to observe some of the same metabolites during the analysis of single beta cells on NAPA. The results obtained for single beta cells were verified by analyzing cell extracts from large cell populations. We have shown the feasibility of directly analyzing ~10 metabolites in a single mammalian cell via LDI mass spectrometry on NAPA. This new technique opens the door for large scale cellular homogeneity studies in diverse fields of biology and medicine.
Do the Sp185/333 immune proteins in the Purple Sea Urchins augment phagocytosis of opsonized bacteria?

The purple sea urchin, Strongylocentrotus purpuratus, a member of the echinoderm phylum is used to study fundamental functions and principles of innate immunity. The Sp185/333 gene family of the purple sea urchins, composed of 40 to 60 loci, is upregulated in response to immune challenge and produces highly diverse mRNAs that encode a wide range of proteins. In response to lipopolysaccharide challenge, ~260 Sp185/333 protein isoforms are present in the whole coelomic fluid (wCF). The wCF is a complex “blood-like” tissue that mediates responses to microbial infections including opsonization, agglutination, encapsulation, and phagocytosis. The coelomocytes (immune cells) are categorized into phagocytes, spherule cells, and vibratile cells, and subpopulations of the phagocytes display phagocytic activity in response to microbial infection. The involvement of the Sp185/333 proteins in the process of phagocytosis was investigated because phagocytosis is an important mechanism to remove and kill microbes. Preliminary data demonstrated that one recombinant Sp185/333 protein, rSp0032, binds to yeast (S. cerevisiae) and marine bacteria (Vibrio diazotrophicus). Because microbial binding is the first step in the process of phagocytosis, we used rSp0032 to see if it could support or augment phagocytosis. Cell-free coelomic fluid (cfCF) was used as the positive control because it contains many opsonins, and artificial coelomic fluid (aCF; a sterile buffer) was used as the negative opsonization control. Preliminary results of the phagocytosis assays show that marine Vibrio opsonized with cfCF induces phagocytosis while aCF does not. Further studies will include opsonization of Vibrio by rSp0032 to evaluate whether it supports phagocytosis. This work only evaluates one of hundreds of variants and it is likely that different variants have different immune effector functions in response to pathogens. Understanding the putative immune functions of the Sp185/333 proteins will advance our knowledge of protein diversity and its importance for innate immunity in an invertebrate.
Measuring Complexity of Models of Mathematical Theories

A mathematical theory is usually given by a set of simple conditions called axioms. For example, Euclidean geometry is a mathematical theory described and determined by five axioms, one of which is “all right angles are equal to one another.” For a given theory, there are many models (a set of elements with certain relations and operations among them) that satisfy the axioms of the theory.

In computability theory we measure complexity of sets of natural numbers using a relative measure called the Turing degree. Namely, we define the relative complexity of two sets $A$ and $B$ as follows: $B$ is more complicated than $A$ if there is an algorithm that decides the membership of $A$ by asking a finite number of questions about the membership of $B$, but not vice versa.

We can encode all information about a countable model, including its domain and relations and operations, in a set of natural numbers. Therefore, we can measure the complexity of structures using the Turing degree. In mathematics, we consider two models to be equivalent if there is a transformation between them, which preserves the relations and operations of the models. We say that these two models are “isomorphic”. The collection of all models isomorphic to a given model $S$ is called “the degree spectrum of $S$.”

We are interested in the distribution of complexity of the degree spectra of models for a given theory. In the 1970’s, Linda Richter of the University of Illinois presented several methods for finding this distribution and gave a number of examples from algebra. Since then many researchers tried to refine her methods and expand the area to new types of algebraic models. Recently, I extended Richter’s line of research to new, non-associative structures. Important examples of such structures are quandles.
Evolutionary Parallels between the immunological molecules of sea urchins and vertebrates

The immune system of vertebrates, including humans, is mediated by a highly defined and specialized suite of cells. The cells of the vertebrate immune system arise (or differentiate) from a single type of stem cell (a non-differentiated progenitor cell). Differentiation is an ordered process that generates a set of functional cell types and is controlled by transcription factors. Transcription factors are proteins that bind to DNA and regulate the expression of specific genes at specific times, thereby controlling and ordering the process of cell differentiation. To begin to understand how the process of immune cell differentiation, or hematopoiesis, has evolved from earlier forms, we have examined the expression of homologues of genes encoding a number of key hematopoietic transcription factors in the organs and immune cells (coelomocytes) of the California purple sea urchin, an invertebrate that is closely related but evolutionarily basal to the vertebrates. Results obtained using reverse transcription PCR (RT-PCR) indicate that many of these transcription factor genes are indeed expressed in the sea urchin, both in the coelomocytes themselves and in the axial organ from which coelomocytes are hypothesized to arise. The axial organ is unique to the echinoderms and, despite a century of investigation, its function remains unknown. The evidence we have gathered strengthens the case for the axial organ as the source of coelomocytes, a role analogous to the thymus, bone marrow or embryonic spleen of vertebrates. In particular, we observe differential expression of hematopoietic transcription factor genes specifically in the axial organ in the presence versus absence of immune activation. Together, these data are the first stage in understanding how the innate immune system of the sea urchin uses genes and proteins similar to those of our own immune system, and a how complex immune systems might evolve from earlier forms.
Effect of ethanol on protein oxidation

Ethanol consumption can have harmful biological effects. The metabolite of ethanol, acetaldehyde, is known to have destructive, deleterious effects in liver cells. The conversion of ethanol to acetaldehyde is done primarily by either alcohol dehydrogenase or the antioxidant enzyme catalase (CAT). The principle function of CAT is to convert two molecules of hydrogen peroxide into water and oxygen. Hydrogen peroxide is a reactive oxygen species produced naturally in a cell that can damage proteins through oxidation and cause them to lose activity. When ethanol is present, catalase reacts with one ethanol molecule and one hydrogen peroxide molecule to produce acetaldehyde, water, and oxygen. We hypothesize that ethanol is a competing substrate for CAT. Therefore, hydrogen peroxide produced by an oxidase (in a model system of CAT, oxidase, and its substrate in a buffered solution at cellular pH) should reach higher levels in the presence of ethanol than in its absence, leading to increased protein oxidation. Data suggest that in this system, the presence of ethanol increases the maximum concentration of hydrogen peroxide reached. We have determined the best way to measure protein oxidation in this system (western blot detection of dinitrophenylhydrazine-tagged oxidized protein) and plan to use this method to measure protein oxidation by hydrogen peroxide in the presence and absence of ethanol. We have also observed that acetaldehyde production increases with increased ethanol addition, and we plan to examine whether or not this leads to increased oxidation independent of the effects of hydrogen peroxide. These experiments can help to better characterize the harmful cellular effects of ethanol consumption.
Immune Cell Proliferation in Purple Sea Urchins

In the purple sea urchin, Stronglyocentrotus purpuratus, coelomocytes are immune cells that respond to injury and infection. Coelomocytes mediate immunological functions and respond to foreign bodies by phagocytosis and encapsulation. To begin to understand the source of coelomocytes, we first questioned whether proliferation of coelomocytes could be documented, a question that has not been addressed previously. Proliferation was measured using 5-ethynyl-2'-deoxyuridine (EdU), a synthetic molecule that is incorporated into DNA in the place of thymidine during DNA synthesis. After injection of EdU into three sea urchins, samples of whole coelomic fluid (wCF) containing coelomocytes were withdrawn over a period of 21 days. The samples were fixed, permeabilized, processed for EdU incorporation using a red fluorochrome, stained for total DNA using a blue fluorochrome, and observed using fluorescent microscopy. We compared the number of EdU-labeled nuclei to total number of nuclei. The level of EdU-labeling gradually increased from day 0 to day 5, followed by a rapid increase in all three urchins after day 5, with a maximum labeling of 18% on day 14. This demonstrated that coelomocytes were proliferating within this time period. From day 14 to day 21, EdU-labeling decreased, possibly reflecting turn-over of new cells and decrease of EdU below the level required for labeling additional cells. However, at day 21 at least 3% of the nuclei remained labeled with EdU. The results illustrate a general pattern for EdU uptake, indicating coelomocyte proliferation, and that EdU labeling is an effective method to measure cell division in marine invertebrates. In future work, we plan to use these preliminary data as a baseline for comparison to coelomocyte proliferation in response to challenge with marine bacteria.
The Production and Consumption of Hydrogen Peroxide by Glucose Oxidase and Catalase

Hydrogen peroxide (H₂O₂) is known for causing oxidative stress and damage to proteins in most cellular systems. To combat this, cells have protective scavenger proteins that consume H₂O₂ and break it down into the less damaging molecules, water and oxygen. This study models these interactions by observing the production of H₂O₂ by glucose oxidase (GOx) and its consumption by catalase (CAT) in vitro. It is important to note that in this model, the production of H₂O₂ exceeds the rate of its consumption (as evident in most cellular systems). This excess H₂O₂ can in turn react with the GOx and damage the protein through oxidization. Experimental methods used in study include spectrophotometric detection of hydrogen peroxide and detection of carbonyl-oxidized protein through immunodetection and 2,4-dinitrophenylhydrazine fluorescence. We find that as GOx catalyzes the formation of H₂O₂ the result is a loss of activity due to oxidation of the protein by its own product. This damage from oxidation increases somewhat linearly over time. In addition, CAT does diminish GOx oxidation but is not completely protective.
Infinite-Dimensional Quantum Computing

ABSTRACT

Category theory has proven promising in capturing the logic of quantum information processing at a fairly high level, in similar fashion to Boolean logic and classical computing. In particular, quantum state evolution and quantum teleportation have been able to be depicted by the category of finite-dimensional Hilbert spaces together with linear transformations. Since all categories behave identically by definition, we can then view quantum computation in a highly intuitive, diagrammatic language. By generalizing the category of finite-dimensional Hilbert spaces to the category of infinite-dimensional Hilbert spaces, we can begin to represent categorically the mathematics of quantum mechanics, which involves observables and bases in arbitrary dimension. We show that this generalization might be achieved by expanding our use of unital Frobenius algebras to nonunital Frobenius algebras and $H^*$-algebras.
Topologically Mixing Tilings of $\mathbb{R}^2$ Generated by a Generalized Substitution

In my poster, I will present a large class of examples of topologically mixing self-similar tilings of the plane. Topologically mixing tiling dynamical systems were investigated by Kenyon, Sadun, and Solomyak. They studied one-dimensional tiling dynamical system generated by substitutions on 2 letters. Given a substitution $\sigma$ with transition matrix $M_\sigma$, they proved that if the lengths of the prototiles are irrationally related, and the eigenvalues $\lambda_1, \lambda_2$ have the property that $|\lambda_1| > 1 > |\lambda_2|$, then the one-dimensional tiling dynamical system is topologically mixing. They were, however, unable to extend there results beyond an alphabet with 2 letters or one-dimensional tilings.

The examples I have studied were first presented by Kenyon in [Kenyon1996]. He proved that any complex Perron number solving $\lambda^3 - p \lambda^2 + r \lambda + q = 0$, $p \geq 0, q, r \geq 1$, is the expansion constant for a self-similar tiling. Solomyak studied general self-similar tilings. He was able to prove that any self-similar tiling dynamical system of $\mathbb{R}^d$, $d \in \mathbb{N}$ is never (measure theoretically) strong mixing. He was also able to prove that any self-similar tiling of $\mathbb{R}^2$ with a complex, non-Pisot similarity is weakly mixing. Solomyak used the construction of Kenyon as examples of weakly mixing tiling dynamical systems of the plane. However, the question as to whether any of these examples are topologically mixing tiling dynamical systems of $\mathbb{R}^2$ remained open. In my research, which was suggest by Solomyak, I have used techniques from developed by Kenyon and Solomyak to prove that an infinite sub-collection of Kenyon's examples are topologically mixing. These are the first known examples of topologically mixing substitution tiling dynamical systems of the plane.
Malaria is a parasitic disease found mainly in areas along the equator and is the 5th leading cause of death for infectious diseases worldwide. A potential new antimalaria agent, 2-iodo-L-histidine, was discovered by NIH researchers to be effective against P. Falciparum, The most lethal malaria parasite. Unfortunately, it is not stable within the human body and is readily deiodinated. The project objective is to see if switching the positions of the iodine substituent and the side chain will cause the molecule to be more robust and prevent quick deiodination in vivo.

Part 1 of the project involved synthesis of 4-iodo-2-methylimidazole and 2-iodo-4-methylimidazole, which are models for 4-iodo-isohistidine and 2-iodo-L-histidine respectively. Stabilities were then checked in the presence of dithiothreitol (DTT), a strong reducing agent, by spotting on a TLC plate.

Part 2 of the project is currently being conducted and involves the synthesis and investigation of the stability of 4-iodo-isohistidine.

It was concluded in part 1 that 4-iodo-2-methylimidazole remained stable while 2-iodo-4-methylimidazole deiodinated under reducing conditions. With confirmation of part 1, the stability of 4-iodo-isohistidine will now be investigated. A positive outcome in Part 2 will be followed by further testing of the agent in vivo by collaborators.
Opitz syndrome is a genetic disorder characterized by birth defects such as cleft lip and palate, and deformities of the brain, heart, and genitalia. This disorder is caused by mutations in the gene that codes for the protein Midline-1 (MID1). Mutations in the MID1 gene hinder a process called ubiquitination, by which MID1 protein is marked for degradation by the cell. The lack of ubiquitination causes MID1 to build up in cells, and may be responsible for the symptoms of Opitz syndrome. I am studying the effects of MID1 mutations on structure and function of the MID1 protein. I am in the process of generating mutations using polymerase chain reaction (PCR), after which I will study functional changes using Western blot analysis, and structural changes using x-ray crystallography and nuclear magnetic resonance (NMR) imaging studies. Using these methods I hope to determine which mutations cause a loss of structure and/or function of MID1, in order to better understand the process that causes Opitz syndrome.
In-Vitro Near-Field Ablation of Biological Samples in the MID-IR Wavelength Region

With the collection of a vast amount of DNA sequences into databases, researchers are realizing that having completely sequenced genomes is not sufficient to explain biological function of an organism. Although DNA is the carrier of genetic information in a cell, proteins do the bulk of the work. They act as catalysts, receptors, and structural components, all of which are required for the life of a cell.

The identification and structural characterization of proteins is now possible through mass-spectrometry-based, soft-ionization techniques. In life science applications, near-field ablation coupled with mass spectrometry is very promising. This is especially promising for the high spatial resolution chemical analysis of various samples in atmospheric pressure.

We will report the ablation of materials like cellulose acetate in water and myoblast cell samples in growth media, with a spot size as small as 1.5micron. These are the first steps towards our goal, to combine atmospheric pressure IR-MALDI with near-field microscopy in order to study protein expression in biological tissue with sub-micron resolution. Often MALDI depends upon a chemical applied to the sample to act as the energy absorbing matrix. With the combination of infrared and MALDI, it is possible to directly analyze cellular samples by using their native water as matrix, and thus perform protein analysis without altering the original spatial distribution of molecules in cell. We will also present the power-dependence of these ablation processes. We found that there is a dramatic increase in the ablation threshold fluences when we go from far-field to the near-field region. We will also report on the difference in the ablation mechanism in air and water medium. This approach has the potential to identify the protein expressed in cells in a relatively non-destructive manner.
Peptide Perturbations in Model Membranes

We investigate peptide interactions with model membranes and how they affect phase dynamics and mobility. Previously, we have studied lipid phase rearrangement due to headgroup cross-linking. Building on this, our current efforts investigate peptide perturbations in lipid bilayers. We cross-link transmembrane peptides on the surface of lipid vesicles to examine the interactions between the helices, mimicking B cell receptor clustering. Expanding on surface-based perturbations, we utilize peptide forming fibrils that associate with anionic lipids, indicating an electrostatic association. These fibril-liposome systems are a useful model to study plaque-based diseases such as Alzheimer’s, Parkinson’s and type II diabetes. We analyze these associations using microscopy, FRAP, FRET and CD spectroscopy.
SE33 profiling: A novel method for allele sequence determination by Triple Primed PCR

Many samples collected for forensic DNA typing are mixtures, which can be very difficult to analyze. The alleles of the SE33 locus are characterized by having a typical 4bp (AAAG) length variation together with a sequence polymorphism, a consequence of an additional hexanucleotide unit (AAAAAG), that occurs once at different locations within the repeat region. Because of this complex repeat pattern, the 58 different length alleles have up to 13 different sequence variations for a total of 171 alleles. Consequently, the SE33 locus has a population heterozygosity of over 90%, making it an excellent marker for mixture analysis and familial testing. We present a novel method for allele determination using triple primed Polymerase Chain Reaction (TP-PCR). In this method, instead of binding to a flanking region, a primer anneals directly to the repeat region during amplification. This will produce multiple fragments of varying length. Because of the unique sequence variation within SE33, with this method alleles of the same length have different electropherogram patterns. This allows for sequence determination without Sanger sequencing. The results of this study demonstrate that allele sequence of the SE33 locus can be determined by PCR.
Unlike classical regimes of physics, nuclear physics does not yet have a complete theoretical description. To scrutinize the validity of theoretical constructions accurate experimental data need to be obtained. Currently, a measurement of the total cross section for $\gamma + n \rightarrow p + \pi^-$ is underway at MAX-lab in Lund, Sweden, using a liquid deuterium target. The resulting $\pi^-$ is detected by its subsequent capture and photoemission by a deuteron through $\pi^- + d \rightarrow 2n + \gamma$. Several large sodium iodide spectrometers detect this emitted photon. Since this experiment deals with an extended target, there are several key quantities that need to be investigated by simulation. The experimental geometry was reproduced in a GEANT simulation where, among other parameters, the fraction of $\pi^-$ s, which do not undergo recapture in the target and the detector acceptances from the extended target were examined. Preliminary results will be shown.

This work was greatly supported by a GW OVPR undergraduate fellowship and DOE grant #DE-FG02-99ER41110
XAS Investigations on Phosphate Poisoning in HT-PEM Fuel Cells

X-Ray Absorption Spectroscopy (XAS) measurements were taken on operating commercially available membrane electrode assemblies (MEA's) in a HT-PEMFC based on phosphoric acid (H₃PO₄) infused polybenzimidazole (PBI) membranes. Two of the MEA's contained a 10% Pt/C catalyst cathode with either 2g or 6g of H₃PO₄ sprayed on the support to investigate the effects of H₃PO₄ concentration on the oxygen reduction reaction (ORR). A third MEA was created with 10% Pt/oxidized multi-walled carbon nano-tubes (MWNT) support and sprayed with 2g H₃PO₄. Operating temperatures were 180°C, 110°C, and 50°C, with H₂ at the anode and synthetic air (O₂:N₂ /1:4) at the cathode.

All in operando XAS data were collected in quick EXAFS mode (4 min.) and analysed using the Dm-XANES analysis technique. The Dm-XANES method takes out the atomic “background” contribution to enhance the contribution due to adsorbates, and then by comparison with theoretical FEFF8 results provides both coverage and binding site information for adsorbates such as (H, CO, OH, H₃PO₄).

As expected the Pt/C(6g) MEA showed considerably more phosphate adsorption than the Pt/C(2g), and the phosphate coverage dropped off with T in all cases. Between 250 and 400 mV, all adsorbed phosphate becomes invisible in the Dm, because like that found previously for adsorbed sulphate, it becomes mobile on the surface until H or OH begin to adsorb forcing the anion to adsorb in specific sites. The O(H) adsorption does not force phosphate off of the surface until well above 800 mV even at 180°C. The Pt/C(2g) and Pt/MWNT(2g) MEA's showed similar PO₄ coverage drop-off with T but above 600 mV at 50°C more OH adsorption occurs leaving less PO₄ coverage on the Pt/C(2g) MEA. This suggests that the oxidized MWNT’s make the Pt-OH bond weaker via a metal-support interaction effect, and therefore MWNT supports might be beneficial to the ORR.
Development of Single Nucleotide Polymorphism (SNP) assays for determination of craniofacial morphology

When a DNA sample collected from a crime scene does not match an STR profile in a state or federal database it serves little purpose without reference samples. Recently assays have been developed for the determination of phenotypic traits, such as eye and hair color from SNPs; these are useful to help direct an investigation or create new leads. The ability to predict craniofacial morphology from a DNA sample to create a ‘molecular identikit’ of the individual could influence investigations beyond basic phenotypic traits. The prediction an individuals' facial morphology could be incredibly influential for criminal investigations and corroborating witness testimony.

In this preliminary study three assays were developed to type a total of 19 Single Nucleotide Polymorphisms (SNP), which are single base changes in the DNA double helix, to determine if certain facial features could be predicted knowing the genotype of an individual at these locations. The assays were developed using Single Base Primer Extension (SBE) also called minisequencing. This methodology targets DNA fragments that are much smaller than those analyzed in conventional forensic DNA analysis, this method utilizes technology, which is already available in crime labs. The SNPs selected were from genes known to be associated with craniofacial development. The selected SNPs are known not to be associated with facial diseases or deformities and could potentially be associated to normal craniofacial variation.

Volunteers were asked to fill out a questionnaire to self assess their facial features. Measurements of the individuals’ face and head were taken, in addition to photographs of the front and profile of their face. Finally buccal swabs were collected from each individual for DNA analysis. Samples will be genotyped using the SNP assays developed and statistical analyses will be conducted to verify the presence of associations between specific SNPs and craniofacial features.
NATURAL SCIENCES

COLUMBIAN COLLEGE OF ARTS & SCIENCES

Development of Recyclable Catalysts for Alcohol Functionalization: Tunable Hydrotalcite Supported Nanoparticles

One of the high priority reactions for greening synthetic routes to active pharmaceuticals involves using unreactive alcohols to synthesize secondary amines. Catalytic alcohol amine coupling has been optimized using several transition metal homogeneous catalysts. Although highly active, these catalysts cannot be typically recovered which limits reaction scale-up. Here we report on the rational development of a recyclable nanocatalyst, consisting of palladium and silver nanoparticles supported on cheap anionic clay, hydrotalcite. Several synthetic hydrotalcites have been prepared with variable composition and surface charge. Palladium and silver nanoparticles have been deposited on the hydrotalcites and characterized by TEM, AFM, Powder XRD, zeta potential measurement and EDX. Their activity for alcohol oxidation, with release of hydrogen, and alcohol amine coupling will be reported. The extensive characterization of this suite of catalysts facilitates rational understanding of the relationship between composition, electronic parameters, nanoparticles size, surface area, and catalytic activity. This approach will be further applied to the design of catalysts for alcohol – CH activation reactions.
NATURAL SCIENCES

SCHOOL OF ENGINEERING & APPLIED SCIENCES

Inducing Vesicle Fusion via Embedded Magnetite Nanoparticles and Magnetic Fields

Using magnetic nanoparticles, we manipulate vesicle mixing. Such behavior is useful for mimicking liposomal docking to the plasma membrane and potential drug delivery. To induce vesicle mixing, we embed iron oxide nanoparticles into the lipid bilayer of vesicles and monitor their effects using fluorescence resonance energy transfer (FRET) to observe vesicle fusion in the presence of an external magnetic field. FRET uses a pair of dyes to show close proximity via photon transfer between acceptor and donor dyes. In this system, we have two separate sets of vesicles ~50-200 nm in diameter. We incorporate a green lipid dye analogue into the first set of vesicles, and in the second set, its orange FRET partner and 5 nm iron oxide nanoparticles. We alter the time vesicles spend in the presence of the magnetic field and then track the increase or decrease of FRET activity to track quantify dye exchange and fusion events. Without nanoparticles, vesicle fusion is not favored. The contribution of the nanoparticles in a magnetic field from the second set of LUVs overcomes the energetic barrier and we observe fusion. In the alternating magnetic field, these vibrating nanoparticles generate heat. We model this thermal energy exchange by considering both Brownian and Neel relaxation mechanisms.

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Sexual assault samples are one of the most common types of evidence that forensic laboratories process. The only undisputable confirmatory test for seminal fluid is the microscopic observation of spermatozoa. However, this technique is time consuming, costly, and has limited automation capabilities. As such, sexual assault evidence is a major contributor to the evidence backlog that laboratories face.

Our objective was to develop a more high-throughput method for the confirmatory identification of seminal fluid using the technique of proximity ligation real-time PCR (PLiRT-PCR). PLiRT-PCR is a protein detection method that uses antibody probes specific for the target protein. A representative DNA molecule is generated when the antigen is present and can then be detected by RT-PCR. PLiRT-PCR is highly compatible with forensic practice because it is sensitive, affordable, amenable to automation, and uses machines that are already present in forensic laboratories.

We have developed PLiRT-PCR assays for prostate specific antigen (PSA) and three sperm specific proteins. PSA is a seminal plasma protein that is important as a presumptive test, particularly for samples that will lack spermatozoa. We detected PSA in a 1:5,000,000 dilution of seminal fluid using PLiRT-PCR, which corresponds to 0.08 – 2.2 pg of PSA. This is 5000 times more sensitive than the immunochromatography tests typically used in crime laboratories. We have also detected two sperm specific proteins using PLiRT-PCR. These two proteins are located on the acrosomal membrane, so we first carried out a permeabilization step to access these proteins. We detected the proteins down to a 1:100 and a 1:1000 seminal fluid dilution, respectively. Detection of these sperm specific proteins indicates detection of spermatozoa. We have thus developed a molecular confirmatory test for seminal fluid that could be automated for high-throughput processing of sexual assault evidence.
Faults and strongly deformed rocks are common in the Blue Ridge province of Virginia and were formed primarily during the amalgamation of the supercontinent of Pangea. Identifying the protoliths (undeformed parent rock) of such exposures is important in field mapping, but is often impossible due to the changes in physical appearance and mineral composition that occur under high strain conditions. Our research focuses on a set of exposures unique in that the transition from undeformed granite to severely, ductilely deformed metamorphic rock is identifiable on the basis of several mineralogical and outcrop scale characteristics. Our goal is to not only reconstruct the history and conditions of an ancient fault zone, but also to better understand the precise mechanisms of deformation. Detailed microscopic analyses indicate that strain along this ancient fault was taken up through the recrystallization of quartz as well as the alignment of micaeous minerals formed during greenschist facies metamorphism, which preceded deformation. Field mapping indicates that basaltic dikes, which are common in this region, accommodated significant strain through development of micaeous minerals during metamorphism followed by development of strong foliation and transposition of planar dikes into direction of strain. The precise timing and rate of deformation are being determined by isotopic geochronology.

Studies of ancient fault zones such as this are important for reconstruction of the geologic and tectonic history of this complex region. Understanding the mechanisms by which ductile deformation occurs and the changes that occur to rocks under these conditions will allow for better identification of rock types in highly deformed terranes. In addition, understanding the fabrics developed by high strain rocks is crucial for the understanding of present day environmental problems as they dictate groundwater flow and are also zones of potential fault reactivation.
Wound healing in the skin is a complex multistep process that necessitates proper movement of cells and their re-synthesis of proteins to replace damaged tissue. A key step in wound healing is the activation of dermal fibroblasts to myofibroblasts with muscle-like properties that provide these cells with the mechanical tension needed for tissue repair. This conversion is regulated by a TGFβ1-mediated cascade that involves the phosphorylation and movement of Smad3 to the nucleus to regulate genes essential in healing, one of which is α smooth muscle actin (αSMA), the key component of myofibroblast stress fibers. This study looked to determine whether the proteoglycan syndecan-1 (sdc1) plays a role in TGFβ1 signaling and fibroblast activation and also asks whether varying concentrations of TGFβ1 influence these events.

Wild type (wt) and sdc1-null primary dermal fibroblasts were grown under serum-starved conditions and then had 0ng/ml (control), 5ng/ml, or 10ng/ml TGFβ1 added. Proteins were extracted either 30 minutes or 24 hours after TGFβ1 addition, and then probed utilizing protein immunoblots and chemiluminescent detection for phosphorylated Smad3 (pSmad3), total Smad3, and αSMA. Comparing the ratio of pSmad3 to total Smad3 in TGFβ1 treated cells, both genotypes responded similarly 30 min after treatment. However, by 24 hours, Smad3 was phosphorylated more in wt cells treated with 10ng/ml TGFβ1. In contrast, αSMA levels increased at both 30 min and 24 hours after TGFβ1 treatment in sdc1-null cells but not wt cells. It appears that while phosphorylation of Smad3 increases over time in cells with or without sdc1, αSMA levels increase more in cells lacking the proteoglycan. αSMA expression in fibroblasts is regulated by canonical (SMAD-driven) TGFβ1 signaling. These data suggest that sdc1 plays a role in mediating the activation of fibroblasts by modulating canonical as well as non-canonical TGFβ1-mediated signaling.
High Performance Computing in Lattice QCD

Electric polarizability is an important parameter for the internal structure of hadrons. It quantifies the ability of the electric field to deform them. Previous studies of polarizabilities have been done at relatively heavy masses, leaving the chiral region largely unexplored. Here we present a study in the background field method, using overlap fermions to probe the chiral dynamics. However, overlap fermions are computationally demanding. We will address the computational challenges we encountered and present preliminary results.
NATURAL SCIENCES

COLUMBIAN COLLEGE OF ARTS & SCIENCES

Neutron emission asymmetries from linearly polarized $\gamma$ rays on natCd, natSn, and 181Ta

Azimuthal asymmetries in neutron yields produced by bombarding targets with linearly polarized photons via $(\gamma,n)$, $(\gamma,2n)$, and $(\gamma,f)$ reactions are being investigated as a possible means of identifying various nuclear isotopes. The High Intensity $\gamma$-ray Source (HI$\gamma$S) at Duke University provides nearly monochromatic, circularly or linearly polarized $\gamma$ rays with high intensity by Compton backscattering free-electron-laser photons from stored electrons. Linearly polarized $\gamma$ rays produced by HI$\gamma$S were incident on natCd, natSn, and 181Ta targets at six energies $E_{\gamma}$ between 11.0 and 15.5 MeV and emitted neutrons were detected both parallel and perpendicular to the plane of polarization by an array of 18 liquid-scintillator detectors at angles in the range $\Theta = 55^\circ - 142^\circ$. Detected neutrons were distinguished from Compton scattered photons by pulse-shape-discrimination and timing cuts, and their energies ($E_n$) were determined using time-of-flight information over a 0.5 m flight path. The characteristic plots of $R_n$, the ratio of neutron counts parallel to neutron counts perpendicular to the plane of the incident $\gamma$-ray polarization, against $E_n$ were constructed for each value of $E_{\gamma}$ and $\Theta$ and then compared to those for other targets studied at HI$\gamma$S, including fissile nuclei 235U and 238U. Experimental results were finally compared to theoretical predictions.
Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), is one of the deadliest infectious diseases. Emergence of drug resistant strains of Mtb and co-infection with HIV has made TB both difficult and expensive to treat. New TB therapies are needed to shorten treatment and be effective against all strains and metabolic states of the organism. Development of inhibitors of 1-deoxy-D-xylulose-5-phosphate reducto-isomerase (Dxr), an essential enzyme for Mtb, is a novel approach toward the development of a new TB chemotherapy. Natural product fosmidomycin inhibits Dxr and kills other organisms reliant on this enzyme. Interestingly, fosmidomycin is not effective against Mtb. The goal of our work is to rationally design small molecule inhibitors that are specific for both of the two major binding sites in Mtb Dxr: the fosmidomycin and NADPH binding sites. Bridging these two adjacent binding sites should yield inhibitors with increased specificity and affinity for Mtb Dxr. The design, synthesis and biological activity of this work will be presented.
Production and Quenching of Hydrogen Peroxide: The Case of Islet amyloid polypeptide (IAPP)

Islet amyloid polypeptide (IAPP), commonly known as amylin, is a 37-amino-acid peptide that is co-stored and co-released with insulin in the pancreas. The normal physiological role of IAPP is not entirely known but it has been shown that the peptide plays a role as a hormone that suppresses gastric emptying, food intake, and glucose homeostasis. In most Type II Diabetes mellitus (T2DM) cases, amylin aggregates and forms fibrils on islet B-cells. Damage to these cells causes T2DM because islet B-cells are the specific sites of secretion and production of both amylin and insulin. The role of this islet amyloid formation in the onset and progression of T2DM is still unknown but studies have shown amylin fibrils to be toxic to cultured islet cells. Environmental factors like oxidative stress can influence the formation of amylin fibrils by causing conformational changes in the peptide. Free radicals and peroxides play a large role in promoting oxidative stress. As a result, this study examines the production of hydrogen peroxide (H$_2$O$_2$) by amylin. The subsequent oxidation of amylin by H$_2$O$_2$ and its potential effect on fibril formation is also a major focus of this research. Published studies have previously claimed that amylin produces H$_2$O$_2$ both endogenously and with the help of copper and reducing agents. Researchers have also confirmed the oxidation of a similar protein, amyloid ß peptide, by H$_2$O$_2$ and have claimed that oxidation influences the formation of fibrils. This study aims to understand the mechanism of H$_2$O$_2$ production by amylin, the potential oxidation of amylin by H$_2$O$_2$ or hydroxyl radicals, the specific conformational changes of amylin during oxidation and the causality between protein oxidation and fibril formation.
We study lipid phase behavior using giant unilamellar vesicles to model cell membrane dynamics. In our system, we investigate the effects of cross-linking in the head groups position via biotinylated lipids, avidin, and its analogues. Cross-linking is the linking of two molecules (biotinylated lipids) via a crosslinking agent (avidin). Vesicles allow us to isolate the lipid rearrangement due to cross-linking, common activity on cell surfaces. By comparing specific binding strength of the coupling and self adhesion, we study the role that cross-linking plays in membrane behavior. Confocal microscopy gives us the ability to visualize the membrane dynamics. Using phase specific dyes, we study the changes that occur with the addition of a cross-linker to the system. Förster Resonance Energy Transfer (FRET) enables us to detect clustering on the submicron scale, beyond the limits of conventional microscopy. Both techniques allow us to quantify the phase behavior due presence of the cross-linking agent. We are developing our FRET analysis to study membrane phase dynamics. Using FRET we detect lipid rearrangement associated with the transition from one-phase vesicles to two-phase vesicles using two different fluorescent dyes, a donor and acceptor. From this simple cross-linking system, we model membrane responses to protein complex formation and oligomerization.
A Comparative Analysis of Social and Breeding Behavior in Kori Bustards (Ardeotis kori struthiunculus) at the National Zoological Park

The Kori Bustard (Ardeotis kori) is a large polygynous African bird – one male mates with multiple females, who then rear chicks independently. Since 1998, the Smithsonian National Zoo has maintained a breeding flock of 1-2 adult males and 2-3 adult females to simulate wild conditions. However, in 2011 the death of two birds reduced the flock to one male and one female. I partnered with Sara Hallager of the National Zoo to study if changes in flock composition produced changes in activity budgets and reproductive behavior. 5 minute scan-based observations and “booming” (courtship display) counts have been collected by zoo volunteers since 2001. These data were compared against 2011 observations to determine what, if any, significant differences occurred. Statistical results indicate that adult males and females have distinct activity budgets, and while courtship display behavior changes each year, there are no significant differences in activities from 2001-2011. Nonetheless, in 2011 behaviors that had never previously been observed, including abandoned clutches of eggs and a truncated booming season, were reported. This suggests that, while activities remain statistically true to pattern, individual breeding behaviors are impacted by changes in flock structure.

The National Zoo is also maintaining a group of sub-adult individuals to eventually supplement the adult flock. Our second objective was to analyze the social structure and activity budgets of sub-adult individuals. A scan-based observation study similar to the adult behavior watch was implemented. Results indicate that sub-adult male and female activity budgets are not significantly different from each other, but are different from adult activities. Sub-adult Kori Bustards are generally more active and participate in a wider variety of behaviors. Several novel interactions, such as object manipulation, were observed. This portion of the study will continue for several years to document the transition from sub-adult to adult behaviors.
Cell Culture Warming: Metabolic Response in Small Populations of Heat Stressed Saccharomyces cerevisiae

Microbial populations frequently encounter large variations in the environmental temperature. Within limits, they are equipped to cope with such an environmental stress. Conventional metabolic analysis requires a large amount of sample (approximately a million cells), as well as a complex sample preparation process, and provides ensemble averages for the cellular composition of the entire population. These averages obscure the often significant variations between subpopulations. The analysis of intracellular metabolites in small cell populations is crucial to understanding cell differentiation, the evolution of phenotypes and interactions with the environment. Laser desorption ionization (LDI) from tailored silicon nanopost arrays (NAPA) for mass spectrometry has been utilized for ultratrace analysis of small biomolecules (as low as a few attomoles) with a wide dynamic range. We exposed small populations (n = ~80) of Saccharomyces cerevisiae (yeast) cells to thermal stress and probed the metabolic changes in order to understand the cellular response. In these studies ~17% of the metabolites in the known yeast metabolome were followed, representing a ~67% coverage of the major biochemical pathways. To find the metabolites responsible for most of the differences between the mass spectra of the heat stressed and standard cell populations, orthogonal projections to latent structures discriminant analysis (OPLS-DA) was performed. Based on this multivariate statistical analysis approach, approximately 40 metabolites were potentially up- or downregulated. Further analysis confirmed that 15 of these metabolites exhibited statistically significant changes in their abundances. Many of the up-regulated metabolites, such as aconitate and glyoxylate, were involved in the glyoxylate cycle (an analogue of the TCA cycle in microorganisms). These research methods and findings can be applied to further explore cellular heterogeneity changes under environmental stress and enhance our understanding of the adaptation of microorganisms.
A majority of Americans would be caught unaware of the astonishing facts about abortion among African American women, and how it is effecting their community. There is an argument being made that the overly disproportionate amount of aborted black babies in the African American community should be considered a form of genocide. Proponents of what is known as the “black genocide” argument base their claim off of what they believe to be the eugenicist and racist beginnings of the Planned Parenthood organization, and that there is a direct connection between the facts about Planned Parenthood, and the outstanding number of abortions occurring in the African American community today.

There are many black and mainstream pro-life groups alike making this argument today, and it is an argument that has lingered since 1960’s. Initially I believed this argument, and thought that if the incredible injustice of genocide was being carried out among my own race, I needed to learn more about it, and fully validate whether it was true.

I began my research with the intent of proving that the “Black Genocide” argument was accurate. I found, while researching the history of Planned Parenthood, the “targeted effort” claims to be invalid. My argument is centered on two core concepts: whether killing the unborn is equivalent to killing a born human, and how one defines genocide. Based on those points, I would be able to distinguish whether this can be considered “Black Genocide” or not. I argue in defense of the pro-life view, but I also argue that genocide indicates intent. Because the Planned Parenthood argument failed, I conclude that this cannot be considered genocide, but rather the genocide rhetoric is used inaccurately by these pro-life groups in order to “shock” more people (blacks especially) into supporting the pro-life view.
Factors in Listeners’ Perceptions of American Dialects and Gender

BACKGROUND
This project aims to relate speech features of dialect and gender by drawing conclusions about which aspects of dialects of American English share more in common with feminine speech, and which with male speech. This paper will identify dialectal speech features and gender speech features, and determine contexts in which gender perception might be influenced by dialect. An interaction between how people perceive a speaker’s dialect and a speaker’s gender could be utilized in communication feminization therapy for male-to-female transgender people.

METHOD
In addition to an extensive literature review, samples of New England English, Standard American English, and Southern American English dialects were phonetically transcribed and compared using the dialect markers most often utilized in the literature to illustrate differences.

RESULTS
In the literature about American English dialects, features such as articulation rate, pause frequency, vowel duration, resonance, and intonation helped differentiate speakers from regions around the United States. Characteristics of speech such as fundamental frequency, intonation, and resonance are currently identified as influencing a listener’s perception of gender and femininity. There are not many overlapping characteristics; however, when listeners identify a speaker’s dialect, they appear to consider gender somehow because gender of speaker is often reported as having an interaction effect with dialect categorization.

CONCLUSIONS
There is some research on how gender affects a listener’s perception of the speaker’s dialect, but little to no evidence of the opposite: how dialect affects a listener’s interpretation of the speaker’s gender. It is possible that the influence of gender on dialect perceptions found to be robust in the literature also applies in the reverse direction. Therefore, future study of the effect of dialect on gender perception is warranted.
Methods to Optimize Inter-Rater Agreement for Ratings of Vocal Femininity

BACKGROUND

Vocal femininity of male-to-female (MtF) transgender clients in voice therapy is typically measured subjectively. Rating scales are commonly used but have a great deal of variability among listeners’ ratings. Shrivastav et al. (2005) attribute poor inter-rater agreement to measurement errors as opposed to true perceptual differences. They proposed that listener variability in rating voice breathiness could be mitigated by requiring listeners to rate stimuli multiple times and then transforming discrete scores into averaged scores and standardized scores. However, Kreiman and Gerratt (2011) did not replicate these findings and attributed the poor agreement to non-random task related factors; that is, differences in perceptual strategies of listeners contribute to variability in perceptual data. This study examines effects of data management in regards to voice femininity rather than breathiness.

1. Does averaging multiple ratings of femininity improve inter-rater agreement? If so, how many ratings should be averaged?
2. Does standardizing ratings of femininity across listeners improve inter-rater agreement?

METHOD

Thirteen listeners (12 female, 1 male) judged the gender of 13 speakers (three male, three female, three MtF transgender, and four FtM transgender) based on two read sentences. Samples were organized into a list, which was repeated ten times with stimuli in randomized order. In addition to discrete ratings of each stimulus presentation, averages and standardized scores were derived and the probability of agreement between pairs of listeners (“Pexact” score) was calculated.

RESULTS

Inter-rater agreement:

1. does not change with additional exposure to the stimuli (near 60% for all 10 repetitions),
2. gradually improves as more ratings are averaged, with diminishing gains after 1st-7th ratings are averaged (75%),
3. decreases slightly when ratings are standardized (near 40%).

CONCLUSIONS

Inter-rater agreement for ratings of vocal femininity collected in clinic or research studies would improve if several ratings of each stimulus were collected and averaged.
The Economics of Healthcare across OECD Countries

This paper looks at the relationship between healthcare spending per capita in OECD countries and respective patient outcomes, which is measured on a mortality/incidence (M/I) basis looking at many illnesses common across OECD countries. OECD countries are used in the analysis of patient outcomes across countries in order to compare the US to countries with similar economies, societies, and government policy. Additionally, the data on healthcare spending in these countries is most readily available as are the incidence and mortality rates from most illnesses. This paper uses empirical data to draw conclusions regarding the efficiency of the US healthcare system with respect to various other systems around the world. Past research has shown that the US has better patient outcomes across various illnesses; however this paper looks to tie the marginal increase in patient outcomes to a cost which is likely to be disproportionately high.
Parental Concern and Perceived Need for School Accommodations Following Concussion: Children with ADHD and/or LD vs. Typically Developing Children

We examined parent-reported concern regarding learning/academic performance following a concussion and perceived need for school accommodations, among children previously diagnosed with ADHD and/or LD and typically developing (TD) children.

PARTICIPANTS AND METHODS

Forty-six concussed children (age 14.1 ± 2.5) with a pre-existing diagnosis of ADHD and/or LD (Mixed Clinical (MC) group) were compared to concussed TD children, matched on age, gender, and race. Parents completed the School Information Sheet as part of a standard clinical assessment. T-tests and Chi-square analyses were performed using SPSS.

RESULTS

Groups differed with regard to the number of previous concussions and pre-existing IEP/504 plans. Parents of TD children showed similar rates of overall concern as those of children with premorbid difficulties. However, there was a trend (p=.075) for MC parents to perceive a greater need for services following the injury than TD parents. Post-hoc evaluation of specific clinical groups suggested parents of children with ADHD had a higher perceived need for services (p≤0.01) than their TD counterparts. More specifically, parents with child with ADHD reported a higher need for extra time (p=0.02).

CONCLUSION

Parents expressed similar levels of concern for learning/academic problems following a concussion, regardless of premorbid level of difficulty. However, preliminary analysis suggests that parents of children with ADHD may have a higher perceived need for academic services. Larger sample size is needed to better compare across clinical groups and control for potential covariates such as pre-existing IEP/504 services and previous concussions. Future research should also examine neuropsychological test performance, recommended school services, and the perceived benefit of services received.
Pre-hospital Medical Services in Cochabamba, Bolivia

This is a study of the largest and best-known ambulance services that exist within the city limits of Cochabamba, Bolivia. These services include public, private, free, and for-profit operations, which combined, account for the majority of pre-hospital emergency health care services that administer care to the inhabitants of Cochabamba. The structure of this work unfolds in the following manner:

The introduction presents the nature and purpose of this study. It depicts the context in which ambulance services operate and objectifies the research. The introduction continues with an explanation of the methodology used to obtain facts, figures, and insight into general conditions. It highlights sources of information and includes the author’s self-analysis of the accuracy of the data as well as potential discrepancies and weaknesses regarding the methods of data collection.

The material obtained from these methods is then presented in three parts. First, a description is given regarding the capabilities and resources available to each ambulance service analyzed. Second, a greater-depth examination into the workings of one particular service, SAR Bolivia, is presented. Third, the manner in which individual ambulance service resources are used in coordination with one another -and their manner of operation in the field at the scene of typical day-to-day health emergencies- is explicated. The study concludes with a general analysis of this reality, as expressed by the paramedics and other emergency health professionals with whom I spoke.
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Indian Biomedicine: The Construction of a Modern Indian Identity

This article presents findings from research conducted in Bangalore, India, investigating the construction of an Indian identity for allopathic/biomedical doctors within the discourse of modernization and traditional revivalism. I suggest a representation for biomedicine that is not strictly ‘Western,’ but rather mutually influenced by Indian culture as well. The doctors who are members of Indian society as well as a ‘Western-educated elite’ are forced to balance their personal and professional identities to create a distinct interpretation of medicine that incorporates the spirituality of everyday culture and the imposed rationality of biomedicine, while maintaining professional legitimacy. Modernization, as applied to the field of medicine, cannot be reduced to a homogenizing force from the West, but rather, it is a distinct, contextually-bound form of biomedicine that reflects a new movement toward a specifically Indian or local form of ‘modernization’. Through participant observation and personal interviews, I provide an in-depth case study exploring the construction of biomedical identities in Bangalore. [key words: medical pluralism, modernity, India, nationalism]
Has the Value of Statistical Life Changed Since the 1990s?

Value of Statistical Life (VSL) estimates are a way to measure the benefits of reductions in death risk in dollars. This study performs a hedonic wage evaluation for risk reductions using the Current Population Survey, Merged Outgoing Rotational Groups (CPS MORG) conducted by the National Bureau of Economic Research and the Census of Fatal Occupational Injuries (CFOI) conducted by the Bureau of Labor Statistics (BLS) for 2003 to 2009. This calculated VSL will be compared to those from older studies using data from the 1990s to see if VSL has changed since the 1990s. It is possible that today’s individuals have changed their priorities to place a higher or lower priority on health and safety, which could generate a different VSL estimate to be used in today’s policy analysis. This is relevant due to the recent interest of creating legislation to dictate the procedure for benefit-cost analyses. VSL estimates are frequently used to quantify the benefits of regulation, for example those made by the EPA, of health gains for individuals. The VSL estimates of this paper range from 8.2 to 12.1 million 2009 USD. The $12.1 million estimate is statistically different from some estimates of older studies, potentially indicating a change in preferences for risk.
COLUMBIA COLLEGE OF ARTS & SCIENCES

Conservatives and Sentencing Reform: Understanding Trends

Appearing ‘soft on crime’ is a perennial problem for politicians. TIME magazine declared that being labelled soft on crime a significant threat to political candidates. The need to appear tough on crime has long driven politicians in general, and conservatives in particular, to advocate harsh penalties for criminals.

Recently, some conservatives have begun to reevaluate their positions on punishment and prison reform. Mark Levin, President of the Landmark Legal Foundation said, “We like arresting people, but it’s getting kind of expensive. [I] t’s not an area where we’re trying to say ‘let’s spend as little as we can,’ the answer is ‘let’s be as cost effective we can.’”2 Alternatives to the standard ‘tough on crime’ position are increasingly popular; on December 15th, 2010, a group of notable conservatives including Newt Gingrich, Edwin Meese, and Grover Norquist signed a statement of principles for criminal justice reform, founding the Right on Crime movement. The group insists that “being a tough-on- crime conservative doesn’t mean the only way to punish people is to ‘lock them up and throw away the key,’”3 and supports a variety of reform positions.

This study investigates the transition from a ‘tough on crime’ position to one that advocates reform. Through the analysis of conservative media, the study explores and scrutinizes the shift in criminal justice and sentencing policy reform and its prevalence in conservative media. The presentation will explore the shifting philosophy of politicians and advocacy groups – with an emphasis placed on the changing views of conservatives and Republicans. Additionally, the presentation will review how sentencing reform has been portrayed by conservative media outlets through by one methodology in particular: a coded examination of coverage and attention that The Weekly Standard and the National Review pay to the issue.

CITATIONS


Museums are “agents of well-being and as vehicles for social change” (Silverman, 2010, pp. 2-3). Museums enrich the quality of individual lives, provide services to communities, and address issues of social justice. The viewing audience in a museum has a role in altering society. Museums can promote this by showing audiences how by-stander effects lead to unintentional discrimination, and encourage pro-social action.

Social action is mediated by a number of variables, including empathy. While empathy has been shown to motivate social action, Trout (2009) suggested that on-going engagement and structured experiences may be necessary to maintain this effect since cognitive biases and forgetting caused by distance are very strong. To address this concern, the researchers of the present study are examining the use of art-based data generated by audiences in response to their visit, triangulated with other instrumentation measured longitudinally.

The United States Holocaust Memorial Museum (USHMM) in Washington, DC, endeavors to inspire individuals “to confront hatred, promote human dignity, and prevent genocide” (2011, para. 1), thereby effecting social action. Thus, the USHMM was selected as an ideal site for testing the study hypotheses: Adult visitors who tour the USHMM permanent exhibition will experience a measurable increase in empathy levels immediately following their tour; and, the visitors who participate in an art therapy protocol will demonstrate increased levels of sustained empathy and activity to effect social change at 2, 7 and 12-month follow up, as compared to adult visitors who do not participate in an art therapy protocol. As this poster will reflect, preliminary results provide tentative evidence in support of the application of art therapy interventions in community settings.
SOCIAL SCIENCES

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Object-based Attention and Prioritization Revealed by the Temporal Order Judgment Method

The human brain is bombarded by a multitude of sensory information all at once. The human visual system copes with this overabundance of information, to some degree, by dividing visual sensory data into a series of distinct objects. It has been proposed that in the absence of an alternative strategy, items appearing on the same object are given attentional priority over items appearing on a different object. Here, we provide strong support for this proposal by using a novel method – temporal order judgment (TOJ). In particular, we demonstrate prioritization for items appearing on the same object as compared to those appearing on a different object. Two target stimuli were presented on the same or different objects and participants reported which of the two stimuli appeared first. One of the targets is generally judged as appearing first, an effect termed as prior entry. It was observed that items appearing on the same object show stronger visual prior entry effects. In the second experiment, we examined whether this same-object prior entry effect is automatic or is a default setting that is abandoned in the presence of an alternative strategy. We modified the paradigm to include twice as many trials with targets appearing on different-objects as those appearing on the same-object. In this version, there was no longer a prior entry effect. These results provide strong support for the attentional prioritization hypothesis, demonstrating that priorities are determined independent of spatial orienting. Additionally, these experiments introduce a novel paradigm for measuring object-based attentional guidance.
 WHAT DOES IT MEAN TO BE AN AMERICAN?

The question has been debated ever since the declaration of America as an independent nation. Early American nationalism has been criticized for excluding minorities in the participation in its collective nationalistic affairs as well as denying minorities the equal membership. African Americans weren’t the only minorities - white men without property and women were barred from participating in sociopolitical affairs such as voting. However, the situation changed over time - the sociopolitical exclusions in which African Americans, poor Whites, and women could not vote were changed: the United States Supreme Court rulings have legalized poll taxes that kept African Americans and poor whites from voting after the ratification of the 15th Amendment in 1870. Women were granted suffrage through ratification of the 19th Amendment in 1920. By looking back through history, the current generation of Americans needs to identify the context of historical information such as the definition of the word American.

 WHAT DOES IT MEAN TO BE AN AMERICAN NOW?

Although the legal terminology to be an American is to hold an American citizenship, I assert that this is not the real definition; I assert that anyone residing in America with a capability to shape the social, political, and economic structure in America is a real American: through time, minorities became real Americans by obtaining real capabilities that shaped America such as voting. In this research I analyze how the American criminal justice system, a factor that has been intensely debated to disadvantage minorities, relates to African Americans on social, political and economic grounds.
Breaking Down the Columns and Building Community: Museums as Facilitators of Civic Engagement

Museums may support citizenship by promoting discussions about public issues through exhibits and programs, creating opportunities for discussion by serving as neutral public settings, or partnering with other community or national organizations to meet specific needs. This research looks to fill a gap about the contemporary meaning of civic engagement in museums and ways in which museums’ programs put this theory into practice. Historically, the term civic engagement has a variety of political, psychological, social, and institutional connotations, but does not specifically address museums. Although many recent museum articles use civic engagement as a buzzword, an agreed upon or synthesized definition remains unclear. With an increasing focus on the role of civic engagement in the missions of museums, a working definition of civic engagement must be adapted to encompass them. Putting civic engagement into a museum context, this research is the launching point for re-thinking museums’ initiatives in a modern world. Utilizing art museums in the nation’s capital as a point of exploration, interviews with prominent leaders in the museum field highlight the extent to which civic engagement is playing a role in their work by identifying key factors such as identity formation and transferrable skills. As seemingly ideal settings for reaching broad audiences, it appears that museums have the opportunity to raise the social platform of any issue, but this is not always a reality. By illuminating barriers that museums face as facilitators of civic engagement, this study is a call to museums to fulfill their revitalized role as community builders and to instill in, and make meaning of objects, individuals, and society as a whole.
Pedophilia: Innate or Developed Disorder?

I will research the issue of pedophilia, and whether it is a developed or inborn disorder. Based on the nature of the disorder, what kind of punishment should child molesters face? If it is an innate disorder, will the punishment be less severe? Along with jail time, should child molesters go through therapy? Should severe punishments like castration be imposed on pedophiles? Generally, how to battle pedophilia?
Many websites collect data about any consumers who visit them. In some situations collection of consumer information is necessary to provide the consumer services, but often such data collection is not necessary. Much of the data collected about consumer online is being sold to data brokers and used to develop target advertisements. Further, companies who use persistent tracking technologies are able to collect data about consumers across several websites. This data is often sold, re-sold, and aggregated to produce comprehensive and detailed profiles about individual consumers. Do Not Track is a movement, web browser feature, and the name of several bills in Congress, all aimed at protecting consumers from the practice of collecting information about consumers online by “tracking” their internet activity.

The rapid development of technologies and the Internet environment pose significant challenges for lawmakers seeking a regulatory solution to online tracking. As a result, successfully regulating will require regulators to look beyond traditional regulatory schemes, such as government regulation or self-regulation. The traditional regulatory frameworks lack the dynamic infrastructure necessary to regulate ever-changing technologies, like those associated with online tracking. My research evaluates four proposed regulatory approaches to online tracking and uses case studies to illustrate the relative strengths and weaknesses of each approach. My research shows that a multi-stakeholder regulatory framework has the greatest potential to be effective in regulating online tracking.
The Path to Food Choices: Deliberative or Automatic?

Prior research has examined menu labeling's effect on food choices, and results have been mixed. This study examined the impact of information on deliberative (caloric information) or automatic (heart-healthy icons) dietary choices. Undergraduate participants (N = 128) were randomized into one of four nutritional information conditions on a menu and asked to select their preferred lunch. The conditions were: 1) a standard menu (i.e., no nutritional information; “Menu N”), 2) a menu with caloric information for all items (“Menu C”), 3) a menu with “heart-healthy” icons next to six low-calorie and six high-calorie items (“Menu H”), and 4) a menu plus both caloric information and heart-healthy icons (“Menu B”). It was expected that: 1) Menu C would lead to significantly lower-calorie meals than menu N. 2) Participants will be more likely to select heart-healthy items with Menu H than with menu C. 3) When given menu B and when the two types of information are incongruent (i.e., high-calorie but heart-healthy), participants will be more likely to select the item than with Menu C. Menu C was not significantly lower in total calories than Menu N (t(1, 31) = 0.74, p > 0.05). Participants were more likely to select heart-healthy items with Menu H than with menu C (t(1, 31) = 1.90, p = 0.06). Next examined is the number of items selected just in the unhealthy (high calorie) items marked with a heart icon (called “Bad” items). Participants did not select significantly more Bad items with menu B than with menu C (c2(1, 31) = 2.33, p > 0.05). Hypothesis two was supported, and hypotheses one and three were not supported. These results suggest that both automatic and deliberative processing may be used in food choices, and that the level of processing may depend on the type of information presented.
Chinese Train Wreck: A Tale of Two Media

Despite China’s sophisticated Internet regulatory system, anecdotes abound of Chinese citizens circumventing government censorship to disseminate political information online that otherwise would have remained suppressed. While case studies and anecdotes paint a compelling picture of how the Internet is changing the information landscape in China, the actual degree to which the Internet is changing the tone, quantity, and content of political information has, so far, received limited empirical investigation. To address this gap, this paper employs content analysis to empirically test whether Weibo, the Chinese Twitter, provided citizens with a different and more critical set of information than that provided by People’s Daily, the Chinese State newspaper, in regard to the 2011 fatal train crash near the city of Wenzhou. This analysis will provide important insight into how the Internet is changing the informational relationship shared by Chinese citizens and their government, which will likely have important long-term implications for China’s political processes and institutions.
The relationship between social collateral within tribes and group withdraw rates in urban ROSCAs

The objective of this research project is to study whether strong social connections will reduce moral hazard within group lending schemes. Specifically, the purpose of this project is to see whether or not there is a greater potential for group lending schemes to break down at a higher rate in urban sectors due to the lack of strong connections and trust within groups. Rotating savings and credit associations, or ROSCAs are informal financial groups that hold regular meetings to pool a predetermined amount of money. At each meeting, one member receives that meetings pool of money, usually to purchase inventory for small businesses, to pay school fees, or to pay rent and food. The member who receives the pool of money rotates every week. The group-lending microfinance model first created by the Grameen Bank was based on these informal ROSCAs. However, ROSCAs and group-lending microfinance schemes will break down if members do not continue to pay their share the weeks after they receive their pool. Therefore, the overall objective of this project is to see if ROSCAs tend to break down in urban sectors due to the lack of strong social connections, and to apply the findings to the possibility of urban group-lending microfinance breakdown in Africa. In order to determine whether or not there is a relationship between social collateral within tribes and group withdraw rates in urban ROSCAs, I will use OLS regressions to run an analysis on whether these variables are correlated or not. Specifically, the expected results for this project is that there is an economically significant positive relationship between the withdraw rates and mixed ethnic ROSCAs in urban Nairobi.
An examination of racial differences in perceived discrimination and health related cognitions

Research shows racial differences in several chronic health outcomes. For example, Black adults are more than twice as likely to be obese, are more likely to have high blood pressure compared to Whites, and have the highest mortality rate for all cancers of any racial and ethnic group (USDHHS, 2012). Research has shown that perceived discrimination is associated with worse self-rated health and health outcomes, supporting the relevance of discrimination on racial gaps between Blacks and Whites in health (Bratter & Gorman, 2011; Pascoe & Smart Richman, 2009). The present study aimed to examine racial differences in perceptions of discrimination in daily life and medical situations, conditional perceived vulnerability to obesity, high blood pressure, and cancer. Racial differences in beliefs related to medical interactions, such as: discounting of medical standards, personal versus professional beliefs about healthy weight, and willingness to accept health information were also assessed. Black and White adults (N = 216) completed a computerized survey assessing these variables. Analyses of covariance, controlling for weight and income, showed that Black participants reported higher levels of perceived ethnic discrimination, medical mistrust, discounting of medical standards, and a bigger discrepancy between weight personally considered healthy and what the medical establishment considers healthy (p< .03). Black participants also reported lower perceived vulnerability to chronic disease if they did not diet or exercise and lower willingness to accept information or referrals from medical professionals (p< .05). Understanding why racial differences exist in willingness to accept information from doctors and perceived vulnerability to disease, as well as discrimination, mistrust and discounting, may provide insight to the roots of racial disparities in health. This insight can inform interventions that may be implemented to eliminate health disparities.
The effects of racial discrimination on the HIV-risk cognitions of African-American young adults

African Americans make up around 13% of the U.S. population, but account for 50% of all new HIV cases (CDC, 2010). The main transmission route for HIV in this population is high-risk sexual contact, behavior that is exacerbated by drug and alcohol use (CDC, 2010; NIMH, 2010). Social exclusion is one of the most common forms of discrimination and is associated with negative psychological outcomes (Smart-Richman & Leary, 2009). The present study examined whether race-based social exclusion impacts health cognitions related to HIV.

African-American young adults were recruited from the D.C. area (N = 110, M age = 22). Participants were randomly assigned to be included or excluded from a group of White confederates of their same age and gender via a modified version of the online ball-tossing game Cyberball. Participants completed a questionnaire measuring perceived discrimination as well as constructs derived from the Prototype-Willingness Model (Gibbons et al., 2003): willingness to use alcohol and drugs, willingness to engage in risky sex, and perceived HIV risk.

Exclusion was attributed to racial discrimination. Controlling for past behavior, age, gender, and relationship status, excluded participants reported 1) higher substance-use willingness (F (1, 109) = 8.06, p = .005, d = .57), 2) higher risky sex willingness (F (1, 108) = 7.46, p < .01, d = .60), and 3) lower perceived HIV risk (F (1, 109) = 6.70, p = .01, d = .59). These effects were replicated substituting perceived discrimination for exclusion condition (ps < .03).

These results demonstrate that perceived discrimination can impact the HIV-risk cognitions of African American young adults, providing evidence of the important role of discrimination in health disparities. This research demonstrates the utility of the Prototype-Willingness model and social exclusion in examining the effects of social cognitive factors on HIV-risk behaviors.