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The Vanderbilt University School of Medicine is firmly committed to training future leaders and scholars in medicine. This includes the ability to recognize and understand the various challenges facing medicine as well as the vision and skill to address these challenges. That’s why we’ve created the EMPHASIS PROGRAM – an opportunity for our students to acquire specialized knowledge and experience in a focused area of their choosing.

The EMPHASIS PROGRAM is a unique mode of self-directed study which takes place during the first two years of medical school. We match the students’ area of interest with those of committed faculty mentors, providing them the opportunity to draw from seasoned professionals. Students cultivate knowledge and skill through these mentorship experiences, as well as hands-on research and study in desired areas of focus.

There are eight EMPHASIS focus areas in which students can choose projects: Biomedical Informatics, Community Health Initiatives and Outreach, Global Health, Healthcare and Public Health Research and Management, Laboratory-Based Biomedical Research, Medical Education, Medical Humanities, Ethics, and Policy, and Patient-Oriented Research. Students choose their areas, mentor, and projects during the fall semester of first year, and then use the spring semester to acquire general knowledge and skills within their EMPHASIS area. During this semester, they also work with mentors to design their studies. All students devote eight weeks to their projects during the first and second year while supported by an EMPHASIS stipend. Projects are completed during the second year and, in the spring; students present their work either as posters or oral presentations at our Spring EMPHASIS Forum.

Students who are part of our Medical Scientist Training Program are also featured in this publication. By the time they have completed the second year of medical school, these students will have selected research areas that will lead their doctoral degrees in biomedical research. The abstracts they have provided will serve as roadmaps for their future full-time doctoral studies.

In this publication, you will find abstracts of all projects carried out by the Class of 2012. The broad range of projects reflects the diversity of interests our students bring them to medical school.
In devising the EMPHASIS PROGRAM, Vanderbilt University School of Medicine sought to channel the diverse skills and passions of our students into the pursuit of scholarship and leadership. Believing that this aim is best achieved in the context of a relationship with a mentor, we sought the assistance of faculty in many different disciplines across the medical school, the university, the community, the country, and the globe. The response has been extraordinarily generous, in terms of both time and commitment. Each student has been able to work closely with a mentor for the duration of the program, spanning the first two years of medical school and including eight weeks during intervening summer. As Director of the EMPHASIS PROGRAM, I want to express my thanks to those who willingly accepted responsibility of mentoring these students. The quality of the work reported in this volume is evidence of the effectiveness of this collaboration.

These 112 abstracts represent the posters that were presented at the EMPHASIS Forum at Vanderbilt University School of Medicine on May 2nd and 3rd, 2011. Of these abstracts, 100 represent the work of students who entered the EMPHASIS PROGRAM in the fall of 2008. Twelve abstracts describe research performed by students in Vanderbilt’s Medical Scientist Training Program.

Consistent with the aims of the EMPHASIS PROGRAM, the topic covered in the abstracts are wide ranging. Students explored innovative projects as diverse as medical informatics and healthcare policy. Students carried out complex, cutting edge laboratory investigations and undertook projects on healthcare delivery in developing countries and among the urban poor.

Many of these projects will be reported at scientific meetings and in peer-reviewed publications. Some students plan to continue to work on their projects as they move to the next phase of their medical education. Others may hand their projects off to the next class entering the program. Regardless of future direction these projects take, it is clear the collaboration between students and mentors has provided significant benefit to students, faculty, and the advancement of knowledge. For many, the opportunity to work closely with a faculty member over the past 18 months has forged a relationship that will endure in the incoming years.

The EMPHASIS PROGRAM is the result of many years of discussion and planning. Once initiated, refinement has continued as we have learned from the experience of students and their mentors. However, if we judge the work presented herein, the overarching goal of nurturing scholarship and leadership in our students has already been successful.
Biomedical Informatics is the scientific field that deals with the storage, retrieval and optimal use of biomedical information for problem solving and decision-making. Vanderbilt Biomedical Informatics is the largest academic department of biomedical informatics in the country, with more than 50 faculty members, a graduate training program, and a portfolio of research and development projects that spans from computational biology and bioinformatics applied to the understanding of biological molecules, through advanced clinical information systems that care for hundreds of thousands of patients at Vanderbilt, to regional health information projects that span many states. Research is focused on all areas of healthcare ranging from computer programs that alert physicians about patient problems to tools that assist basic scientists with bench research. The students’ educational focus is in three general areas of biomedical informatics:

1. Developing, evaluating and refining the computer tools available to clinicians caring for patients.

2. Using computer applications and techniques to better enable clinicians to assemble evidence for patient care and research.

3. Managing biologic or genomic information in ways that support discovery of new therapies or that guide basic science research.

“It has been very exciting to observe students as they learn about the field of biomedical informatics. We have had students with a wide range of technical backgrounds who have made landmark contributions to the field. The Emphasis Program is facilitating an exchange of knowledge among our medical students, our faculty, and our graduate students, in a way that has enhanced the intellectual capabilities of all three groups.”
MEDICAL RECORD KEEPING IN THE SUMMER CAMP SETTING

JAYCELYN HOLLAND

BIOMEDICAL INFORMATICS

BACKGROUND PROBLEM
According to the American Camp Association (ACA), approximately 10 million children attend camp each summer. Many of these campers will require healthcare while they are at camp, which, due to the environment, presents its own unique set of challenges. The ‘wilderness’ setting often limits access to technology, and parents are not present during the provision of care, thus increasing the importance of health histories provided by parents at the beginning of the summer.

OBJECTIVES
Many studies have documented the rates of illness and injury at summer camp as well as the content of health histories provided by parents, but there is less information available concerning the state of medical record-keeping in this setting. We are hoping to obtain a general sense of how documentation is carried out in the camp healthcare setting as well as evaluate the use of a web-based survey for summer camp research.

MATERIALS AND METHODS
In order to better understand the storage and use of health information concerning campers, a survey is in the process of being distributed to camps accredited by the American Camp Association via the REDCap system. Information will be obtained concerning the use and availability of technology, as well as documentation of care provided at camp.

CONCLUSIONS
Our plan is to continue distributing the survey, possibly using a paper-based format, in an attempt to increase our response rate.

ACKNOWLEDGEMENTS
American Camp Association; M. Deborah Bialeschki, Ph.D. – Director of Research Barry A. Garst, Ph.D. – Director of Program Development and Research Application Committee for the Advancement of Research and Evaluation

MENTOR / DEPARTMENT
Dr. Trent Rosenbloom Dr. Stuart Weinberg Biomedical Informatics

UPDATING PEDIATRIC GROWTH CHARTS FOR PATIENTS WITH DOWN SYNDROME – A MULTI-CENTER STUDY

STEPHANIE HSU

BIOMEDICAL INFORMATICS

BACKGROUND PROBLEM
Growth charts have become an integral part of standardized patient care. The transition to electronic health records (EHR) systems allows healthcare providers to easily track and chart development in pediatric populations. Most importantly, deviations from the normalized curve are recognized as early indicators of secondary medical, social, and/or psychological factors. Unfortunately, pediatric subpopulations with divergent growth patterns from the unaffected population do not have equivalent, electronically accessible growth charts.

OBJECTIVES
Our study focused on the Down syndrome population whose development is still currently monitored using paper-based charts published by Cronk et al in the 1970’s. Advancements in surgical, nutritional, and supportive care since then have altered the prognosis and development of Down syndrome patients, making these charts largely outdated. Based on successful preliminary studies completed with Vanderbilt data, we organized a multi-center data collaboration to generate updated, electronically accessible growth charts for Down syndrome patients.

MATERIALS AND METHODS
An email was sent to various pediatrics listservs during summer and fall 2010 to gauge interest from outside institutions in contributing patient data to our database. We organized a team of Vanderbilt specialists and resources necessary to support this study.

CONCLUSIONS
We will begin data processing later this year and plan to have preliminary charts for distribution within the year. Afterward, we will distribute the initial charts to participating centers for feasibility and feedback. We will work with the centers to adjust the charts before finalization, publication, and distribution. We plan to have both paper and electronic versions of the chart for easy implementation into both paper-based and electronic health record systems.

ACKNOWLEDGEMENTS
Tracy L McGregor, MD Qingxia (Cindy) Chen, PhD Angel Qi An, MS Hui Nian, MS William D. Dupont, PhD

MENTOR / DEPARTMENT
S. Trent Rosenbloom, MD, MPH (Department of Biomedical Informatics (DBMI))

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VANDERBILT UNIVERSITY SCHOOL OF MEDICINE - EMPHASIS PROGRAM - FORUM VI - MAY 2011
Through the Community Health Emphasis Program, medical students develop a substantial set of products that address an unmet community health problem. As they do this, they develop skills in community leadership and scholarship, and helping patients practice positive health behaviors. Students receive training from Center for Health Services in community research strategies including focus groups, in-depth interviews, community needs assessments and grant writing. Nonprofit organizations serve as community partners, helping students develop a strong relationship with the community.

Community Health Emphasis Enduring Understandings
• The health of the community plays a critical role in the health of the individual.
• Health may be strongly influenced by a person’s physical, social, political, economic, psychological, or cultural environment
• You think you know the full answer, but you don’t. There are non-medical explanations, resources, and solutions to consider.
• Successful community health programs are interdisciplinary, built from the community level up.

Community Health Emphasis student projects may address
• Health risks/diseases that disproportionately affect underserved populations.
• Obstacles to health and healthcare for the underserved.
• The socio-cultural, historical and medical aspects of caring for an underserved population.
• Principles, approaches and skills needed by medical providers in an underserved community.
• Skills and strategies that motivate patients to practice positive health behaviors
• Diagnosing the health needs of a community and designing plans to meet those needs.

“These students who selected Community Health were, not surprisingly, advocates by nature. They demanded the support of the school in full measure, so that community people would not be left behind in the excitement over bench research or more glamorous emphasis areas. Thus group of Community Health Emphasis students are brilliant, energetic, and helpful to each other step of the way. It was pure pleasure to work with them and to share in their pride as their objectives were met, their papers were accepted for publication, they achieved funding for their community projects, and in some case, became award winners for service to the community.”

Barbara Clinton, M.S.W. is Director of the Center for Health Services at Vanderbilt University. Ms. Clinton is an Adjunct Assistant Professor in both the medical schools and nursing schools at Vanderbilt and has worked as a counselor, a community organizer and therapist with children. Ms. Clinton helped a system of alternative health services for seniors for the state of Georgia and has served as an advisor to the former Vice President Al Gore, the Tennessee Commission on Aging, the National Center for Children in Poverty at Columbia University, the Appalachian Rural Science Initiative of the National Science Foundation, and several private foundations.
OBJECTIVES
Although the disparity in clinical trial participation is well documented, the main reason why African Americans and the medically underserved do not participate in cancer clinical trials (CCT) has not been agreed upon. New policies and initiatives are required to ensure minority access to CCT and applicability of subsequent results from CCT.

BACKGROUND PROBLEM
More than 30% of Tennesseans are currently obese. In a previous Emphasis study, 50% of South Nashville residents were found to travel two hours round trip to the closest available major fresh foods source. The physical barrier to accessing a supermarket or local produce vendor can reduce fruit and vegetable intake by 32%. Moreover, adults living in neighborhoods with a supermarket and/or grocery store had rates of obesity nearly half that of adults with access to only convenience stores (21% versus 32-40%).

OBJECTIVES
1. To increase the availability of and access to healthy foods in identified food desert neighborhoods in Nashville, TN. 2. To decrease the costs of healthier foods for food desert communities to fair market prices. 3. To educate community members in food deserts of healthier recipes for the management of chronic conditions. 4. To determine the effect of access to healthy foods on food purchasing behavior in food deserts.

PRODUCTS DEVELOPED
With a $65,000 grant from The Frist Foundation, a 28-foot trailer was retrofitted with shelving and refrigeration to provide a mobile option for groceries to seven food desert neighborhoods in South and East Nashville. An expansion to an additional seven sites will be completed by September 2011.
BRIEF DESCRIPTION
A non-profit social enterprise venture was created to increase access to healthy foods in the South, East, and North Nashville communities, to educate community members about healthy nutrition, and to determine the actual need for access to healthy groceries in the community.

CONCLUSIONS
There is an adequate market demand for a sustainable business to be created to supply healthy foods in the food desert communities of Nashville. The cost of healthier foods is not a limiting factor for low-income neighborhoods as SNAP benefits provide a large market share and prices can be significantly reduced as overhead is limited. Nutrition education needs to supplement the creation of access for healthy foods to initiate an effective behavior change model in food deserts.

ACKNOWLEDGEMENTS
The Frist Foundation, Organized Neighbors of Edgehill, Vanderbilt University, Jill Flowers, Community Food Advocates

MENTOR / DEPARTMENT
Dr. Robert Miller, VUMC; Jim Schorr, Owen Graduate School of Management; Barbara Clinton, VUMC.
The Global Health focus area targets health problems in resource-limited settings, including diseases of poverty and the tropics, and provides students with opportunities to learn first-hand about health issues of international significance. Research projects span a broad range of themes in global health, from medical sciences and clinical investigation to socio-cultural correlates of health and health care delivery. Projects in this area fulfill the practicum requirement of the Vanderbilt Institute for Global Health’s Graduate Certificate in Global Health.

The primary objective of the Global Health component of the Emphasis program is to nurture a growing number of students interested in global health issues, helping them to assess and understand some of the most pressing public health issues of our time in their socio-economic and culturally specific context. The Global Health focus area serves to introduce these students to the fundamental principles of service, research, planning, and management methodology in resource-limited settings. Our program has fostered the enthusiasm of approximately 60 students who have elected to participate in Global Health in the past five years. A number of students have published their work in international peer-reviewed journals or in more informal ways for general audiences. Students must plan early because overseas projects have increased complexities to obtain final approvals.

Douglas Heimburger
Dr. Heimburger directs the Education and Training portfolio of the Vanderbilt Institute for Global Health (VIGH) and conducts research on nutritional influences on antiretroviral therapy outcomes in HIV/AIDS. Before joining VIGH in 2009, Dr. Heimburger served on the faculty of the Departments of Nutrition Sciences and Medicine at UAB, where his titles included Senior Scientist in the UAB Clinical Nutrition Research Center, Center for AIDS Research, and Comprehensive Cancer Center; Director of the Clinical Nutrition Fellowship Program; and Associate Director of the UAB Sparkman Center for Global Health. During a Fulbright Scholar award-supported sabbatical in Zambia in 2006-7, he initiated nutrition research in a population of Zambians starting antiretroviral therapy for HIV/AIDS. He has served on the Advisory Board of the Fogarty International Center (NIH), the governing Council of the American Society for Clinical Nutrition, a standing Review Group for the National Cancer Institute, the U.S. FDA’s Food Advisory Committee, and a Test Materials Development Committee for the United States Medical Licensing Examination.
OPTIMIZATION OF NEUTRALIZATION ASSAY IN SEROPREVALENCE STUDY OF DENGUE VIRUS INFECTION IN PREGNANT WOMEN IN NORTHERN ARGENTINA

KATHARINE BURNS
GLOBAL HEALTH

BACKGROUND PROBLEM
Dengue fever epidemics occur in tropical countries throughout the world as a result of mosquito transmitted infection. The four viruses, DENV 1, 2, 3, and 4, cause disease ranging from mild dengue fever to a severe hemorrhagic fever/shock syndrome. The prevalence of each dengue virus varies between regions affected by epidemics. A seroprevalence study can shed light on the characteristics of the geographic distribution of infection and the clinical manifestations of a susceptible population in the region.

OBJECTIVES
To optimize the neutralization assay using DENV 1, 2, 3, 4 local virus isolates to describe the seroprevalence of those strains in pregnant women in Northern Argentina.

MATERIALS AND METHODS
The peripheral blood was obtained from consenting mothers who visited hospitals in the provinces of Misiones, Salta, and Catamarca in N. Argentina. The neutralization protocol was conducted using serial serum dilutions and then confronted with each virus strain in a 24-well plate format. We used Vero cells and a 1% methylcellulose overlay with a crystal violet stain for plaque visualization and counting.

CONCLUSIONS
Optimization of an antibody neutralization assay allows for the uniform processing of patient samples on a mass scale with consistent results. These assays can generate information concerning the seroprevalence of an emergent dengue fever epidemic within a certain time frame in a specific region of the world.

ACKNOWLEDGEMENTS
Dra. Laura Talarico, Dra. Natalia Reynoso, and Juan Pio Batalle of Fundación INFANT, Buenos Aires; ASTMH Benjamin H. Kean Traveling Fellowship; VUSM Overall Fellowship

MENTOR / DEPARTMENT
Fernando Polack, M.D., Division of Pediatric Infectious Diseases at Vanderbilt, Executive Director at Fundación INFANT, and Guillermina Melendi, M.D., Fundación INFANT

SURVEY OF PATIENT OPINIONS ON OPT-OUT HIV TESTING IN THE GPHC A&E

APRIL CHRISTENSEN
GLOBAL HEALTH

BACKGROUND PROBLEM
Opt-out HIV testing in the ED has the potential to detect a substantial number of undiagnosed infections. Patient acceptability of this type of testing in this setting has not been studied in Guyana.

OBJECTIVES
The primary objective was to determine the percentage of patients who would assent to opt-out testing and contrast the characteristics of those who would assent versus those who would decline. The second objective was to assess potential reasons for why people would not accept. Materials and Methods A convenience sample of 352 non-critical adult patients who presented to the GPHC A&E were enrolled. The subjects were interviewed to determine whether or not they would assent to opt-out HIV testing in the A&E. Demographics and reasons for declining testing were obtained.

CONCLUSIONS
This study shows that a majority of those presenting to the Georgetown Public Hospital A&E would accept opt-out HIV testing if provided. Over a third had not yet been tested, and 2/3 of those indicated they would be willing to accept testing. The high ranking of fear-associated questions as a reason to decline testing evidence that although high proportions of Guyanese are being tested, discrimination or perceived discrimination is still persistent. Lack of knowledge on HIV education was not a significant barrier.

MENTOR / DEPARTMENT
Dr. Stephan Russ, Vanderbilt ED, Dr. Seth Wright, Vanderbilt ED, Dr. Navin Rambaran, GPHC A&E

RISK FACTORS FOR BRONCHOPULMONARY DYSPLASIA IN BOGOTÁ, COLOMBIA

ANNA L FAHY
GLOBAL HEALTH

BACKGROUND PROBLEM
The estimated incidence of bronchopulmonary dysplasia (BPD) in the United States is approximately 30% for premature infants with birth weights less than 1000g. Very little is known about the incidence and epidemiology of BPD in developing countries like Colombia.

OBJECTIVES
To determine the incidence of BPD in Bogotá, Colombia and to assess for potential modifiable risk factors associated with this outcome.

MATERIALS AND METHODS
We conducted a retrospective chart review of infants 35 weeks and less gestation admitted to Hospital Universitario San Ignacio from January 2008-May 2010. A pre-designed data collection sheet of relevant risk factors for BPD was used to extract data from two databases: the hospital electronic medical record and a specialized Kangaroo Mother database. Data was de-identified and simultaneously entered into a RedCap database. BPD was defined as the need for supplemental oxygen greater than 28 days. Chi-square and Wilcoxon tests were calculated comparing infants with and without BPD.
CONCLUSIONS
We observed an abnormally elevated incidence of BPD in this relatively mature population of infants despite adequate exposure to antenatal steroids and surfactant. We hypothesize that altitude (elev. 8,530 ft) may play a role in the incidence of BPD in this setting due to a prolonged transition period with increased pulmonary pressures. This could explain the observed increased need for supplemental oxygen, ventilatory support, and surfactant therapy.

ACKNOWLEDGEMENTS
Emily E Maston, Juan G Ruiz, Juan M Lozano, Mario A Davidson, The Overall Foundation

MENTOR / DEPARTMENT
Dr. Mario Rojas, Department of Neonatology

GENDER-SPECIFIC DIFFERENCES IN THE PROTECTIVE EFFECT OF BREASTFEEDING IN ACUTE RESPIRATORY ILLNESS

KATHERINE KUDYBA
GLOBAL HEALTH

BACKGROUND PROBLEM
Acute respiratory illness (ARI) is the leading cause of hospitalization for infants worldwide. Males present with ARI more often and with a more severe illness. Breast milk contains several factors that may enhance infant immunity or contribute to the development of immature lungs. There is compelling evidence that breastfeeding is protective against severe respiratory infections and death, however the literature is conflicting. Interestingly, it has been shown that the protective effect of breastfeeding parallels the gender differences in the burden of ARI, with breastfeeding inferring protection females but not males.

OBJECTIVES
(1) To describe the burden of ARI and breastfeeding practices between genders. (2) To determine the benefits of breastfeeding between male and female infants.

MATERIALS AND METHODS
A prospective viral surveillance was conducted in children admitted with respiratory symptoms and/or fever to a major hospital in Amman, Jordan between 3/2010 and 4/2011. Enrollment criteria included; < 6 months of age and diagnosis of bronchiolitis, bronchopneumonia, or pneumonia. Clinical data was collected by parental interviews and medical chart review.

CONCLUSIONS
Further studies are needed determine if indeed breastfeeding has an effect on the development of ARI and if it varies between gender.

ACKNOWLEDGEMENTS
Collaborators: Ryan Lang Lindsey Lawrence Mario Davidson

MENTOR / DEPARTMENT
Natasha Halasa MD MPH, Pediatric Infectious Disease Najwa Khuri-Bulos MD, Dean of Research Jordan University

EXTREME VITAMIN D DEFICIENCY IN A COHORT OF JORDANIAN INFANTS

RYAN D. LANG
GLOBAL HEALTH

BACKGROUND PROBLEM
A high prevalence of vitamin D deficiency has been reported in India, Bangladesh, and selected Middle Eastern countries including Iran and Pakistan. However, the current prevalence of vitamin D levels in newborns in Amman, Jordan is unknown.

OBJECTIVES
To determine the prevalence of vitamin D deficiency in selected Jordanian full-term newborns and risk factors associated with low levels.

MATERIALS AND METHODS
This was a prospective cohort study which enrolled infants ≥37 weeks of age and born within 96 hours at Al Bashir Hospital in Amman, Jordan. Mothers reported if they smoked and/or were exposed to smoke during pregnancy. Child’s birth weight, average daily number of hours mother spends outdoors, and heel-stick blood samples for vitamin D measurement were also collected.

CONCLUSIONS
The prevalence of severely low vitamin D levels in newborn infants in Amman, Jordan is substantial, despite these newborns being born during the spring and summer months. Vitamin D supplementation is needed in this population.

ACKNOWLEDGEMENTS
The Vanderbilt Institute for Global Health provided fellowship support for this project through the Overall Fellowship Program to support overseas travel and research. Additional support comes from the UBS Optimus Foundation and the Vanderbilt Institute for Clinical and Translational Research grant support program (1 UL1 RR024975 from NCRR/NIH) for REDCap support.

MENTOR / DEPARTMENT
Dr. Natasha Halasa – Department of Pediatrics, VUMC; and Dr. Najwa Khuri-Bulos – Department of Pediatrics, VUMC; and Department of Pediatrics, Jordan University Hospital

PERCEIVED STRESS IN PREGNANT WOMEN IN RURAL SOUTHWEST INDIA

VANESSA NEWTON
GLOBAL HEALTH

BACKGROUND PROBLEM
Pregnancy can be stressful for a woman. During pregnancy, maternal stresses can range from daily hassles and pregnancy related hassles to major life events, like the illness of a child or abuse by a family member. These maternal stresses during pregnancy are known to have adverse consequences, both for the mother and for the unborn baby. Previous studies have
linked high maternal stress with increased activity of the Hypothalamic-Pituitary-Adrenal (HPA) axis, increased release of stress hormones (ACTH, CRH and cortisol), and greater incidence of preterm labor. These previous studies, however, sampled African American women and Scandinavian women. This study is the first to look at the relationship between maternal stress in South Asian women, specifically Indian women, and selected biological outcomes, therefore emphasizing mental health as an important aspect of ante-natal care.

OBJECTIVES
This study aims to assess the perceived stress level of pregnant women in villages surrounding Mysore, India, and to correlate the perceived stress level with anemia, demographic information such as income, education level, and age, and birth outcomes. An additional objective is to correlate one characteristic of stress, which is a woman’s fear of giving birth to a girl child, with anemia, demographics, and satisfaction with the sex of the child, if the woman gave birth to a girl. This characteristic of stress was hypothesized to be related to lower income, lower education, and older age of the pregnant woman.

MATERIALS AND METHODS
Perceived stress was measured using a validated 30-question stress scale and was administered by a female Indian counselor and employee of the Public Health Research Institute of Mysore, India. The stress scale is a measure of whether the situations in one’s life are appraised as stressful. The scores are taken on a continuous scale so that the higher the score, the higher the stress level of the woman. The scale was established by a group of experts including a psychologist, psychiatrist, sociologist, gynecologist, and researchers in reproductive health. The stress scale was found to be both reliable (alpha reliability coefficient of 0.83) and valid (correlation coefficient of 0.63; P<0.01). Lab values were obtained by a nurse and research technician employed by the Public Health Research Institute to measure anemia status. Overall, 662 pregnant women participated in the study, from 62 villages surrounding Mysore. Descriptive and univariate analysis were calculated and a multivariable regression model was fitted.

CONCLUSIONS
Although total maternal stress was not statistically significantly associated with anemia, demographics, or birth outcomes, further studies of culturally sensitive measures of maternal stress should be performed. Fear of giving birth to a girl child is a stressor to many women in India, and is rooted deeply in cultural and religious traditions for preference of a male child. Due to this preference for giving birth to a male child, female infanticide in India is rampant and misuse of ultrasounds in sex-selective abortions is also a common challenge for healthcare workers. Despite the Indian government making it illegal for sex determination by ultrasound in 1994, the law has not been strictly enforced and combination of female infanticide and sex-selective abortions have led to a distortion of the national sex ratio, which in some areas near Mysore is 861 females for every 1000 males.

ACKNOWLEDGEMENTS
Purnima Madhivanan, MBBS, MPH, PhD; Mario Davidson, PhD

MENTOR / DEPARTMENT
Douglas Heimburger, MD Vanderbilt Institute for Global Health

LIMITED EFFECTIVENESS OF SCHOOL-BASED DEWORMING IN RURAL KENYA
LAURA S. PETERSON
GLOBAL HEALTH

Background Problem
In 2007, the rate of intestinal helminth infection in primary school aged children in a particular village in rural Southwestern Kenya was estimated to be more than 68%. Since then, these same school children have been treated with 400mg albendazole every three months.

OBJECTIVES
This study is a return to the same area three years later to estimate the current parasite burden.

MATERIALS AND METHODS
Examination of fecal samples from primary school children by direct wet mount smears for the ova and larvae of all intestinal helminths, including Ascaris lumbricoides, Hookworm, Strongyloides stercoralis, Trichuris trichuria, and Schistosoma mansoni

CONCLUSIONS
There was a decrease of approximately 24% in the prevalence of intestinal helminths in primary school children in this village since 2007. Although this decline is substantial, the overall prevalence, at 44%, is still significantly too high. Methods other than chemotherapy, such as health education and sanitation campaigns, must be considered to adequately reduce levels of intestinal parasitism in the community.

ACKNOWLEDGEMENTS
Thanks go to Michael Ondiek, Denis Omondi, John Badia, Drs Sten Vermund and Johanna Riesel.

MENTOR / DEPARTMENT
Douglas Heimburger, Vanderbilt Institute for Global Health

THERAPEUTIC ALLIANCE: SATISFACTION AND ATTRITION OF PATIENTS IN A MENTAL HEALTH CLINIC IN PERU
MARIA C. PROM
GLOBAL HEALTH
BACKGROUND PROBLEM
Neuropsychiatric disorders are among the top three burdens of disease worldwide, and contribute to a significant amount of time lost to disability in low-income nations. However, little to no support is offered to those suffering from mental illness in these nations, and patients who find assistance often discontinue treatment long before reaching an adequate level of functioning. The reason for patient dropout from mental health treatment programs in low-income nations is under-researched due to limited resources dedicated to evaluating mental health programs.

OBJECTIVES
This study examines one of the leading reasons for patient drop-out in high-income nations to determine if program improvement methods currently utilized in those nations can be applied to decrease the early patient drop-out in low-income nations.

MATERIALS AND METHODS
The strength of the patient-provider relationship and patient satisfaction with the treatment program were examined via the Working Alliance Inventory (WAI) and Patient Satisfaction with Services questionnaires after one appointment with a psychiatrist or psychologist at a free mental health clinic in Ayacucho, Peru. Measures of satisfaction and strength of patient-provider relationship were compared between patients who did or did not return for their second visit within three months. Demographics and other characteristics of the patients were also compared, as well as clinical experience, treatment style, occupation, and gender of the treating clinician.

CONCLUSIONS
The results of this study will be utilized to establish methods of intervention in clinical and treatment techniques to prevent future patient attrition.

ACKNOWLEDGEMENTS
Luis Bedregal, MD, Yale University Department of Psychiatry James Phillips, MD, Yale University Department of Psychiatry Mario A. Davidson, PhD, Vanderbilt University Department of Biostatistics Commission for Mental Health of Ayacucho

MENTOR / DEPARTMENT
Jeffrey Stovall, MD, Department of Psychiatry

IMPLEMENTATION OF HEALTH PASSPORTS IN A RURAL CLINIC IN LWALA, KENYA

TINA SHAH
GLOBAL HEALTH

BACKGROUND PROBLEM
Medical records are instrumental in maintaining continuity of care by conveying a patient’s pertinent social, medical, and treatment history to a health care provider. Although the Lwala Community Health Centre in rural Kenya has seen over 30,000 patients since opening in 2007, the centre does not have a fully functioning record system to document and store the medical histories of its patients. Difficulties in timely record retrieval, storage and legibility have rendered the current medical records obsolete as clinicians are often unable to review a patient’s past medical history before providing him or her with care.

OBJECTIVES
To introduce a new tool in patient care, health passports adopted from national clinics in Malawi were translated and modified to fit the care provided at the Lwala Centre.

MATERIALS AND METHODS
The passports were introduced through clinical staff meetings that were held to discuss the passports and provide education on their function and potential benefit to both the staff and the patients. The contents of passport were modified over several weeks to engender maximum use and efficiency by the clinicians. Additionally, the concept of patient held records was introduced as a way of reducing record retrieval time and storage for the centre while enabling the patient to take his or her medical record on a visit to a different health centre. A pilot study of 130 patient held health passports was conducted with a 3 month follow up on whether the patient brought back the passport on subsequent visits to the clinic.

Conclusions
The centre has since decided to institute clinic held health passports and has administered over 4000 passports since June 2010.

ACKNOWLEDGEMENTS
Eric Manders, Ph. D Vanderbilt Institute for Global Health Frederick Ochieng, M.D. Lwala Community Alliance

MENTOR / DEPARTMENT
Douglas Heimburger, M.D. Vanderbilt Institute for Global Health James Nardella, M. Ed. Lwala Community Alliance

MORTALITY AND CONGENITAL HEART DISEASE SURGERY IN PEDIATRIC PATIENTS IN COSTA RICA

MICHAEL STOKER
GLOBAL HEALTH

BACKGROUND PROBLEM
Little is known of the survival rates after congenital heart disease (CHD) surgery in developing countries, including Costa Rica. A pediatric cardiothoracic program was established in 1964 in Costa Rica but no formal evaluation of the program has taken place.

OBJECTIVES
The aim of the study was to determine the risk-adjusted mortality in the pediatric cardiothoracic program in Costa Rica, to determine the risk factors for mortality, and to compare those
results with contemporary CHD surgery outcomes in the USA and Guatemala.

MATERIALS AND METHODS
This is a retrospective study of patients 18 years of age or younger who underwent CHD surgery at the National Children’s Hospital in Costa Rica from January 1st, 2000 to December 31st, 2005. Data generated by a systematic and random chart review was stored in a computerized, secure database. The risk adjustment for congenital heart surgery (RACHS-1) method was used to adjust for case mix. Results were compared to the databases from the USA and Guatemala.

CONCLUSIONS
In-hospital mortality was abnormally elevated in patients undergoing CHD surgery in Costa Rica. High rates of low cardiac output and hemorrhage in non-survivors with a shorter length of stay suggest that the mortality is related to events in the immediate post-operative period. As a result of the study, a cardiac care unit is being created with additional surgical staff and nurses dedicated to cardiac care.

ACKNOWLEDGEMENTS
Marc G. Cribbs, M.D., M.S., Mario A. Davidson, Ph.D., Abdon B. Castro, M.D., Mario A. Rojas M.D, M.P.H. Vanderbilt University, Nashville, TN, USA. Hospital Nacional de Niños, Dr. Carlos Sáenz Herrera San José, Costa Rica.

MENTOR / DEPARTMENT
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IMPACT OF THE 2010 FIFA WORLD CUP ON EMERGENCY DEPARTMENT WORKLOADS AT THREE CAPE TOWN PUBLIC HOSPITALS

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GLOBAL HEALTH

BACKGROUND PROBLEM
Mass gathering events pose a unique medical and public health challenge. Host cities for events such as the FIFA World Cup must engage in significant pre-event planning to prepare Emergency Medical Services and hospital Emergency Medical Departments appropriately.

OBJECTIVES
The purpose was to perform an audit of Emergency Department (ED) workloads in Cape Town public hospitals during the month of the 2010 FIFA World Cup (June 11 to July 11, 2010) compared to the same month the previous year (June 11 to July 11, 2009).

MATERIALS AND METHODS
Data was collected from ED patient registers at nine Cape Town hospitals, although only three (Somerset Hospital, Victoria Hospital, and Helderberg Hospital) have been included in this report due to incomplete records. Data points included the number of patients who entered the ED, the number of male and female patients, the number of children and adults, assigned triage colors, basic types of presenting complaints, and patient destinations after being seen.

CONCLUSIONS
Overall, the 2010 FIFA World Cup appears to have had little impact on the numbers of patients presenting to the Emergency Departments of Victoria and Helderberg Hospitals. About half as many patients visited Somerset ED in 2010 compared to the same month in 2009, although this may largely be due to the fact that on match days patients were diverted from Somerset to other hospitals due to its proximity to the Green Point Stadium. Even on non-match days, however, Somerset ED still saw many fewer patients per day on average compared to 2009.

ACKNOWLEDGEMENTS
Dr. Lee Wallis; Dr. Kirsty Cohen; Dr.

W. TYLER WINDERS
GLOBAL HEALTH

BACKGROUND PROBLEM
Human respiratory syncytial virus (RSV) is the leading cause of lower respiratory tract infections in children less than 1 year of age and is an important cause of respiratory tract infections in other populations such as the immunocompromised and elderly. By the age of 2, almost all children have had exposure to RSV with peak incidences in the winter or rainy seasons.

OBJECTIVES
The purpose of this study is to assess RSV rate reporting variability and identify potential trends and factors influencing the reported incidences.

MATERIALS AND METHODS
A Medline search was performed using the following inclusion criteria: acute respiratory tract infections, subjects must be less than 18 years of age, and the purpose was not to evaluate treatment or prophylaxis. Required variables include: season, inpatient vs outpatient setting, subject age, method of surveillance, duration, RSV detection method, and location. 329 papers were identified, and 126 met inclusion criteria.

CONCLUSIONS
RSV reporting rates are problematically variable. Trends demonstrated here display that RSV incidences are lower in less...
developed countries. While this may be the case, other explanations such as a lack of funds, experience, and technology seem more plausible. RT-PCR is more sensitive to RSV than viral culture and immunofluorescence, but the results indicate that the method of detection is not the causative factor of the rate variability. Other possible sources of variability include viral trends over time, publication bias, and differing diagnostic criteria for respiratory infections.

ACKNOWLEDGEMENTS
Dr. Buddy Creech, Dr. Fernando Polack, Dr. Kimberly Crimin

MENTOR / DEPARTMENT
Dr. Buddy Creech; Pediatric Infectious Diseases
Melissa McPheeters, PhD, MPH, Assistant Professor of Obstetrics and Gynecology and Medicine and Public Health, is Co-Director of the Vanderbilt EPC, Deputy Director for Women’s Health Research at Vanderbilt, and Co-Director of the Vanderbilt CTSA Database core. In addition to her research as a healthcare epidemiologist, Dr. McPheeters has more than 15 years of experience in the translation of research to practical and useful products. Dr. McPheeters’ PhD, completed in 2003, was in healthcare and reproductive epidemiology, with an emphasis on the use of epidemiologic analytic methods in large databases - she has continued this work over the past seven years, focusing on expanding approaches to analyses in administrative data, such as hospitalization data, as well as large-scale weighted surveys. Dr. McPheeters is an expert in comparative effectiveness reviews and on epidemiologic study design and analysis, with content expertise in maternal and child health. She has worked at the CDC and at state government in addition to her academic career so brings a strong public health perspective to her work.

Sunil Kripalani, MD, MSc, is Associate Professor in the Department of Medicine, Chief of the Section of Hospital Medicine, and Associate Director of the Effective Health Communication Program. He is an academic hospitalist whose research concerns hospital-based communication, with a focus on transitions of care, health literacy, and medication management. Dr. Kripalani has expertise in the performance of observational research studies (surveys, qualitative research, and secondary data analysis), as well as intervention studies (quality improvement interventions and randomized controlled trials) to inform and improve patient care. His research in health literacy and hospital medicine has been recognized nationally, and he enjoys mentoring medical students and post-doctoral trainees.

The student experience in the area of Healthcare and Public Health Research and Management is designed around a research track or management track. Students in the research track complete a hypothesis-driven investigation in a field of healthcare research, such as health behavior and education, epidemiology, or outcomes research. Common research methods in this area include chart review, patient surveys, database analysis, qualitative research, systematic review, and clinical trials. The management track involves a healthcare management internship and quality improvement project, in which the student works as part of an interdisciplinary team to improve an aspect of patient care.
BIVA: A NOVEL METHOD FOR NUTRITIONAL ASSESSMENT IN PEDIATRIC CANCER PATIENTS

KATHERINE ALLEN

HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Pediatric cancer patients are at substantial risk for changes in nutritional status due to perturbation of energy balance, which increase risk for infection and death and decrease chemotherapy effectiveness. Current methods of assessment do not allow for adequate monitoring. They primarily rely on changes in a person’s weight, which often occurs after metabolic and functional changes have already occurred. Additionally, changes in nutritional status based on weight alone do not allow us to determine the nature of the weight change (i.e. muscle, water or fat).

OBJECTIVES
This study aims to ascertain if Bioelectric Impedance Analysis (BIA) can be used as a nutritional assessment (NA) tool in pediatric cancer patients and to examine how it compares to more conventional NA methods.

MATERIALS AND METHODS
BIA measures impedance, which is a combination of resistance, $R$ (function of intra & extra cellular fluid volume) and reactance, $X_c$ (function of the dielectric material of tissue cells). BIA was measured in 49 patients and plotted as a BIVA graph ($X_c/H$ vs. $R/H$). Height and weight data were collected and BMI for age percentiles were calculated. Linear mixed effects models were used to analyze association between BMI &BIVA.

CONCLUSIONS
BIVA appears to be a useful NA tool in pediatric cancer patients. Similar to BMI, it was able to identify severely cachectic patients.

MENTOR / DEPARTMENT
John B. Pietsch, Pediatric Surgery

PREVALENCE OF RISK FACTORS FOR ATRIAL FIBRILLATION - CAN WE IDENTIFY HIGH-RISK EMERGENCY DEPARTMENT PATIENTS?

STEPHANIE A. COUCH

HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
The Framingham Heart Study identified clinical factors associated with an increased risk for developing atrial fibrillation (AF). Trials have shown promising treatments to delay the onset of AF.

OBJECTIVES
Evaluate the frequency of these known risk factors in a cohort of emergency department (ED) patients on visits prior to their AF diagnosis.

MATERIALS AND METHODS
We conducted a retrospective, observational cohort study and systematic chart review of the electronic medical record (EMR) at a university tertiary referral center. ED patients who were newly diagnosed with AF between 7/1/05 and 8/31/08 and had visits to our ED prior to their diagnosis were included. We documented the presence of the risk score variables (age, sex, body-mass index (BMI), systolic blood pressure (SBP), hypertension treatment, PR interval, and ages of clinically significant cardiac murmur and heart failure diagnosis). We calculated the patient’s risk score for each visit prior to their AF diagnosis.

CONCLUSIONS
Nearly half the patients diagnosed with new AF had risk factors reported on prior ED visits. The ED provides an opportunity to identify patients at high risk for AF, provide education, and refer them for primary prevention interventions.

ACKNOWLEDGEMENTS
Cathy A. Jenkins, Alan B. Storrow

MENTOR / DEPARTMENT
Tyler W. Barrett, MD MSCI Vanderbilt Emergency Department

TYPE 2 DIABETES MELLITUS AND OBESITY ARE INDEPENDENT RISK FACTORS FOR POOR OUTCOME IN PATIENTS WITH HIGH GRADE GLIOMAS

LAILA HASSAM-MALANI

HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
High Grade Gliomas (HGG) are common malignant brain tumor in adults. They have an average overall survival of 12-36 months. By studying prognostic factors, physicians can better stratify risks in both a clinical and research setting. Authors have demonstrated that Diabetes Mellitus (DM), hyperglycemia, and obesity are risk factors for poor outcomes in patients with systemic malignancies, but these potential risk factors are poorly characterized in patients with brain tumors.

OBJECTIVES
To demonstrate that DM and elevated BMI are independent risk factors for decreased progression-free survival (PFS) and overall survival in patients with HGG.

MATERIALS AND METHODS
We conducted a retrospective cohort study of 171 patients with HGG. Information was extracted from the electronic medical records, and records of preexisting DM and BMI at the time of presentation were obtained from the medical history. The independent association of DM and BMI with overall survival and progression free survival were assessed via multivariate proportional-hazards regression analysis. Variables associated with
BACKGROUND PROBLEM
Substance abuse (of both alcohol and other mind-altering drugs) amongst practicing and training physicians has been a growing concern. Addiction is seen as a public health concern for both physicians and their patients.

OBJECTIVES
This project evaluated the risk factors for substance abuse amongst Vanderbilt University School of Medicine students.

MATERIALS AND METHODS
A survey was conducted from December 2008 to January 2009 of 301 first, second, and third year students that collected demographic characteristics as well as data to evaluate risks for mental health disorders. Validated instruments such as the MAST and DAST scores were used to measure eating disorders, depression, state and trait anxiety, and alcohol and drug abuse.

CONCLUSIONS
In agreement with other studies of medical students, we found no association between substance abuse and other psychiatric disorders. This could imply that the factors behind addiction development in the general population (comorbidity with other psychiatric disorders) may differ from those in medical students (more stress related). We found race, sleep habits and religious beliefs to be significantly associated with substance abuse. However we believe gender was the only variable to have practical importance in the medical student population. This is an area that could warrant further investigation.

ACKNOWLEDGEMENTS
Sweta Ghodasara, Samantha Martin, Melissa McPheeters, Denis O’Day

MENTOR / DEPARTMENT
Mario Davidson (Biostatistics), Scott Rodgers (Psychiatry) Center
STATINS AND WOUND CLOSE IN ELDERLY BURN PATIENTS

ELLIOTT KIM
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
A primary concern in patients with large burns is sepsis and wound exposure. A significant portion of the body can be exposed without a skin barrier until complete wound closure which may lead to greater risks of infection. Prolonged wound closure can also lead to longer durations within a hospital.

OBJECTIVES
We have previously shown that premorbid statin use is significantly associated with decreased mortality in burn patients. In this study, we examined the effect of premorbid statin use on number of days to complete burn closure, as noted on inpatient or outpatient charts.

MATERIALS AND METHODS
Our previous retrospective cohort of 223 patients age 55 and over, admitted to VUH Burn Service from January 1, 2006 to December 31, 2008, yielded 96 patients who met the criteria of having open burn wounds on admission and were followed until burn closure was complete.

CONCLUSIONS
Prior statin use is not associated with a significant difference in time to wound closure in elderly burn patients.

ACKNOWLEDGEMENTS
Vanderbilt Burn Unit

MENTOR / DEPARTMENT
Dr. Mary Fogerty - Department of Trauma

PATIENT PREFERENCES AND SELF-SELECTION IN AN ORTHOPAEDIC RANDOMIZED CONTROLLED TRIAL

JAKE MCCLURE
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
MeTeOR is a multi-center, randomized controlled trial (RCT) comparing operative and non-operative treatment of meniscus tears in knees with osteoarthritis. This NIH-funded RCT will finally answer the question of optimal treatment for these complex patients with multiple causes for knee pain. Therefore, ensuring the external validity of the results and the integrity of the findings is crucial. Thus, we used a unique dataset available at the Vanderbilt site to compare baseline characteristics of patients choosing to enroll in MeTeOR with those that refused enrollment.

OBJECTIVES
Our primary objective was to ensure that the results of the MeTeOR study are applicable to the general population. By more clearly defining the study population using data unique to Vanderbilt, we could investigate possible differences between those refusing enrollment and those enrolled.

MATERIALS AND METHODS
All eligible patients were stratified based on their preference regarding MeTeOR, and those refusing enrollment were further separated into those preferring surgery and those preferring rehabilitation. We hypothesized that more active patients, younger patients and those working full-time would forego enrollment in MeTeOR and subsequently prefer operative treatment. Using electronic medical records at VUMC, we collected baseline characteristic data including age, sex, degree of joint space narrowing by Kellgren-Lawrence grade (KLG), pain and mechanical symptoms, occupation, education, Marx activity level, and SF12 scores. Differences in these baseline characteristics were analyzed between the groups outlined above.

CONCLUSIONS
Using this more inclusive dataset of baseline characteristics, we have demonstrated that there are no significant differences between those enrolling in MeTeOR and those refusing, thus strengthening the results and conclusions that will be drawn from this RCT.
ACKNOWLEDGEMENTS
Cameron T. Atkinson MD, Kurt P. Spindler MD, Warren R. Dunn MD MPH, Emily K. Reinke PhD

MENTOR / DEPARTMENT
Kurt P. Spindler, MD; Vanderbilt Orthopaedic Institute

NOISE INDUCED HEARING LOSS: A CONCERN FOR OR STAFF?

MATTHEW MCDONALD
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Concerns raised over noise created in the OR during surgery suggest a lifelong risk of obtaining Noise Induced Hearing Loss (NIHL). Sound Pressure Level (SPL) is the metric used to correlate sound with its risk of inducing NIHL. Very little SPL data from surgical procedures have been published.

OBJECTIVES
Our goal was to collect SPL data of surgical procedures conducted in the Vanderbilt ORs and compare it to known SPL thresholds for NIHL and current OSHA regulations.

MATERIALS AND METHODS
SPLs (broad band and 1/3 octave band) were measured in each operating room using a professional sound level meter (SLM) placed at ear level on the anesthesia cart. SPLs were recorded on the A-weighted scale using the slow SLM setting. SPL data was matched to the surgical procedures occurring during each data collection period as defined by the procedure start and stop times as recorded in the electronic medical record. Data from each surgical procedure was categorized based on the surgical specialty of each procedure. The Leq (equivalent sound level) was calculated for each procedure and then compared to known thresholds for increased NIHL risk and OSHA regulations. Describe methods and materials used in the research or project.

CONCLUSIONS
Data collected demonstrate little concern for NIHL as predicted by average noise levels created during surgical procedures. However, great variation in susceptibility to NIHL among individuals cannot rule out zero risk of NIHL from surgical OR noise. Furthermore, SPLs created in any closed environment are highly dependent on environmental dimensions, contents, and noise sources. Potential risk of NIHL may vary based on individual OR factors including instruments, tools, and people working within it.

ACKNOWLEDGEMENTS
Jeremy Federman

MENTOR / DEPARTMENT
Michael Pilla Department of Anesthesiology

COMPARISON OF NEUROCOGNITIVE OUTCOMES AFTER HYBRID CORONARY REVASCULARIZATION VERSUS STANDARD CABG SURGERY

LAUREN MIOTON
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Hybrid revascularization combines the techniques of standard coronary artery bypass graft (CABG) surgery with percutaneous coronary intervention (PCI) into one setting, thus allowing physicians to simultaneously utilize PCI and CABG. Neurocognitive complications after standard CABG significantly increase perioperative mortality and hospitalization time, and can lead to a decrease in the patient’s quality of life.

OBJECTIVES
To compare the postoperative neurocognitive outcomes of patients who had standard on-pump CABG with those of patients who had hybrid revascularization.

MATERIALS AND METHODS
Preoperative, intraoperative and postoperative information was gathered from the electronic medical records of patients who had hybrid coronary revascularization and patients who had standard CABG from April 2005 – July 2008 at Vanderbilt.

CONCLUSIONS
Our results show no statistical difference in the incidence of neurological complications between the hybrid and the standard on-pump CABG groups. Thus, hybrid coronary revascularization is both safe and feasible.

ACKNOWLEDGEMENTS
The American Association for Thoracic Surgery Natalia Solenkova

MENTOR / DEPARTMENT
John Byrne, M.D., Marzia Leacche, M.D.; Department of Cardiac Surgery

QUALITY OF LIFE IN PATIENTS WITH OSTEONECROSIS AFTER CANCER TREATMENT

DAVID MOORE
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Treatment for Acute Lymphoblastic Leukemia (ALL), the most common childhood malignancy, has allowed survival rates to rise above 85%. Current treatment relies heavily on high dose corticosteroids, leading to significant morbidity among survivors. Perhaps the most debilitating complication is Osteonecrosis (ON), affecting more than 10% of ALL patients, and upwards of 45% of patients receiving bone marrow transplants (BMT). Other risk factors for ON include increasing age and graft versus-host-disease (GVHD).

OBJECTIVES
This project is the first step toward a larger goal of being able to predict which patients are at risk for developing ON and at what
stage of their treatment. Before this can be done, it must be shown that ON causes patients to incur a significantly lower quality of life.

MATERIALS AND METHODS
This is a retrospective case controlled study and survey. Thirty ALL patients that developed ON were identified and matched with 65 ALL patients with no diagnosis of ON. Patients were screened to ensure standardization of treatment, and then SF-12 quality of life surveys were sent to all patients.

CONCLUSIONS
This study, aside from highlighting the limitations of survey research, revealed that future prospective studies at Vanderbilt should limit themselves just to the ALL and AML patient populations. Because of the rarity of this disease, a multi-center study design may need to be considered.

MENTOR / DEPARTMENT
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DOES THE PRESENCE OF A HAND SURGEON TRANSLATE TO CALL COVERAGE?
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HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Shortage of emergency hand care is an emerging problem as hand specialists limit their on-call hours. Patients with hand trauma are often transferred from hospitals known to have qualified hand surgeons.

OBJECTIVES
This study evaluates the discrepancy between elective and emergency hand coverage in Tennessee.

MATERIALS AND METHODS
All 119 hospitals in TN with both an emergency department and operating room were contacted via a telephone survey.

CONCLUSIONS
Our results strongly support the need for increased emergency hand coverage. Possible solutions include multi-hospital coordinated call schedules, regional hand centers, and increased incentives for call coverage.

ACKNOWLEDGEMENTS
Dr. Vic Zaydfudim, Dr. Bruce Shack

MENTOR / DEPARTMENT
Dr. Thayer, Department of Plastic Surgery

DOES CALLING “1-800-QUIT-NOW” IN THE EMERGENCY DEPARTMENT HELP PATIENTS QUIT SMOKING?
MICHAEL PELSTER
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Smoking is a public health epidemic. Although numerous Emergency Department (ED) smoking cessation interventions have been studied, few, if any, have been shown to have consistently positive effects on quit rates.

OBJECTIVES
To our knowledge, this study is the first to examine the use of the federally-administered smoking cessation resource, the National Smoking Cessation Quit Line (NSCQL), in the ED. We hypothesized that introducing ED patients who smoke to the counselors on the NSCQL would significantly increase the odds of smoking cessation at follow-up.

MATERIALS AND METHODS
Patients identified as current smokers were approached for enrollment after the initial evaluation by the treating physician. After consent was obtained, the patient was randomized to either the placebo arm, where no active intervention was conducted, or to the intervention arm, where a researcher called the NSCQL from the bedside and placed the subject in immediate contact with a counselor. Exclusion criteria included patients unable to provide consent or deemed unstable or inappropriate to enroll by the attending physician. Follow-up data were collected by phone or mail approximately two months after enrollment.

CONCLUSIONS
Using the 1-800-QUIT-NOW line in the ED is a quick, easy, and effective way to help ED patients who smoke to kick the habit. Our study is limited by being a single-center study, and our results need further validation in other states and institutions.

ACKNOWLEDGEMENTS
Vanderbilt University Department of Emergency Medicine, Brett Bechtel, MD, Jim Fiechtl, MD, Laurie Hawkins, Meredith Sellers

MENTS / DEPARTMENT
Mentor: Benjamin Heavrin, MD, MBA—Department of Emergency Medicine, Statistician: Cathy Jenkins—Department of Biostatistics

REVAMPING PRIMARY CARE DELIVERY: A PATIENT-CENTERED MEDICAL HOME APPROACH FOR HYPERTENSION
MICHAEL POKU
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
The current system of ambulatory care delivery provides sub-optimal value in light of overall costs. Repeatedly, the literature highlights the poor performance around quality outcomes across multiple populations and conditions. Ineffective management of chronic conditions such as diabetes, hypertension and congestive heart failure, often cause short and long term adverse health events such as stroke, myocardial infarctions, renal failure and a host of other costly complications. Review of the literature on managing patients with these chronic illnesses illustrates that our system is far from optimally designed. Much of the inefficiency
results from the lack of an evidence-based, reliable, patient-centered plan of care, as well as the overall lack of the necessary people, processes, technologies and structure (payment systems and culture) to truly engage the patient and manage to that plan of care to quality. With respect to hypertension specifically, the lifetime risk in the United States is 80%-90% while less than half of hypertensive patients demonstrate adequate blood pressure control. To address deficiencies that exist in current models of outpatient care Vanderbilt University Medical Center has created the My Health Team at Vanderbilt (MHTAV) pilot model, a quality improvement approach that brings together concepts from the medical literature including medical home, telemedicine, the chronic care model, business operations, informatics literature, and our own personal experience in patient engagement and team-based care towards defining a pilot to test a transformative new model in ambulatory medicine. It is designed to create a system to address the limited capacity and fragmentation of the current health care model. The first task of the MHTAV program was to optimize the management of hypertension.

OBJECTIVES
The MHTAV pilot program was created to optimize the chronic care management of patients with hypertension in light of JNC 7 guidelines. This study reports the initial results with respect to patients enrolled in the pilot program between April 1, 2010 and February 23, 2011 with evidence of uncontrolled hypertension in-clinic at their initial visit.

MATERIALS AND METHODS
A before-after matched-pair analysis was conducted on a non-random sample of adult primary care patients enrolled in the MHTAV program with uncontrolled hypertension at time of enrollment into the pilot at 3 months post-enrollment. Criteria for enrolling patients into the MHTAV program included medication-treated hypertension; this study focused on that subset of enrollees whose blood pressure was not at goal upon enrollment into the pilot. A comprehensive care plan was created with input from the patient, physician, and care coordinator during the initial clinic visit and each patient had a blood pressure goal established based on JNC 7 guidelines with age and co-morbidity adjusted goals; a subset of these patients had their blood pressure goals modified by the care team for practical care management reasons. All patients utilized clinic-verified home blood pressure cuffs that they were each taught to use during the initial clinic visit. Patients submitted blood pressure readings to care coordinators on a regular basis (the care team began recording these readings for study purposes in 09/2010). For each enrolled patient, care coordinators served as the point person to engage patient and care team, combat clinical inertia, address treatment failures, and initiate therapy escalation between and during visits until patient’s home blood pressure is at goal. Patients were contacted by members of the care team at least once a week until goal blood pressure was achieved. Patients’ blood pressure was considered to be “in-control” (and thus attaining goal pressure) when at least 75% of readings (minimum 12 readings) over at least a 21-day period met JNC 7 guidelines (this protocol was developed based on the most recent literature). In the event that a given patient failed to submit regular blood pressure reports, said patient was contacted by clinic coordinators and encouraged to submit their blood pressure measurements in a more timely fashion; if the care team did not have the minimum of 12 readings to evaluate a given patient’s blood pressure over a particular period the last blood pressure assessment was carried over. Once a patient’s goal blood pressure was achieved, said patient was considered to be in-control. In-control patients had their blood pressure re-assessed at a minimum of either 3 months after achieving their goal for those patients considered to be “high-risk,” or a minimum of 6 months after achieving control for all other patients. Moreover, a host of care protocols, patient dashboards, population analysis tools, and other EMR tools were created for data management and clinical management support. The in-clinic systolic blood pressure at enrollment was compared to the same measure (when it was available) in a matched-pair analysis during 3-month return visit.

CONCLUSIONS
Patients enrolled in the MHTAV pilot program with evidence of uncontrolled hypertension in-clinic at enrollment saw significant declines in their systolic pressure measures at 3 months after joining the new initiative. Likewise, a majority of these patients were able to achieve blood pressure control at home within 3-months of enrolling into the pilot program. The initial results from this pilot suggest that advanced care coordination (including medication titration and lifestyle interventions administered between clinic visits), encouraging patient engagement/empowerment, the use of specially-tailored EMR tools, and a proactive approach to address treatment failures and prevent clinical inertia may significantly improve a given hypertensive patient populations’ blood pressure. However, in order to be sure the results seen in this pilot study are valid (e.g. to ensure the drop in systolic pressure wasn’t a mere regression to the mean effect) the sample size needs to be larger and the study protocol must be refined to minimize bias (e.g. ensuring consistent data points for all patients at the same intervals, developing a workable model to
study home blood pressures in order to avoid a biased effect of using in-clinic measure such as white coat hypertension or masked hypertension, including a control group). At any rate, if the MHTAV pilot program cost-effective and scalable the approach it teaches may provide a model for enhanced care management for patients with hypertension. Additional patients and consistent data points across time are needed to draw more complete conclusions.

ACKNOWLEDGEMENTS

MENTOR / DEPARTMENT
Bill Gregg (dept of medicine, dept of bioinformatics); Jim Jirjis (dept of medicine, dept of bioinformatics); Michael Bowen (dept of veterans affairs, dept of medicine); Josh Peterson (dept of medicine, dept of bioinformatics, dept of geriatric research education and clinical center).

SERUM LEVELS OF METHYL METHACRYLATE FOLLOWING EXPOSURE DURING ORTHOPAEDIC PROCEDURES
MEREDITH SELLERS
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Polymethylmethacrylate (PMMA) is the major component of bone cement used in orthopaedic procedures. Previous research in lab animals exposed to high levels of PMMA indicated that the compound has teratogenic effects, and these studies influenced the current recommendation that pregnant operating room personnel scrub out during cementing. However, no studies in humans have definitively proven that inhalational exposure to PMMA in the operating room setting has toxic effects.

OBJECTIVES
To determine whether and how first & second eye cataract surgery result in significant improvement in VR-QOL.

MATERIALS AND METHODS
Retrospective analysis of the 25-Item National Eye Institute Visual Function Questionnaire (VFQ-25) from the VA Ophthalmic Surgical Outcomes Database. The VFQ-25 was administered pre- & post-operatively to first eye (N=60) & second eye (N=19) cataract surgery patients to assess VR-QOL in terms of 11 function-specific subscales & a composite score. A “staged bilateral” group (N=44) underwent first & second eye operations but only completed questionnaires before the first operation & after the second, with no questionnaires in-between.

CONCLUSIONS
Data shows statistically significant incremental increase in most categories of VR-QOL from first to second eye surgery. First eye surgery does not improve VR-QOL significantly more than second eye surgery. Data from second eye & bilateral surgeries indicates that further cataract surgery can improve VR-QOL in ways that first eye surgery alone cannot.

ACKNOWLEDGEMENTS
Dr. Amy Chomsky, MD Dr. Chun Li, PhD

MENTOR / DEPARTMENT
Dr. Amy Chomsky, Vanderbilt Eye Institute

BRAIN INJURY IN THE ADOLESCENT AND ACCESS TO CARE
ENOCH SIZTO
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Brain injury (BI) is the leading cause of death in adolescents and may
led to long-term debilitation. Improved outcomes are associated with cognitive therapy. Barriers to care in trauma populations are well-described and, in pediatric oncology patients, regional differences in access to care have been identified in treatment seekers.

OBJECTIVES
Our objective is to identify patterns of prevalence of brain injury in adolescents, and describe reported difficulties in accessing specialty care.

MATERIALS AND METHODS
We conducted a cross-sectional analysis of data from the 2007 National Survey of Children’s Health (NSCH), conducted by the CDC, to be representative at the state and national levels, comparing adolescents with reported BI to those without. Covariates examined as potential confounders were selected on the basis of clinical and statistical significance. Multivariate logistic regression was conducted to examine the association between report of having a BI and report of difficulty accessing specialist care.

CONCLUSIONS
The 2007 NSCH identified approximately 3.3% of adolescents having ongoing issues with brain injury. There appears to be difficulty accessing specialty care with obvious regional differences identified, most notably the Western region. Poor general health and no medical home were associated with this disparity.

ACKNOWLEDGEMENTS
Jeff Seroogy, Shanthi Krishnaswami

MICHAEL STOCKIN
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
Traumatic brain injury (TBI) is the leading cause of death and disability following injury worldwide. The standard scale for TBI severity is the Glasgow Coma Scale (GCS). Most patients are given two GCS scores before treatment: one in the field and one upon admission.

OBJECTIVES
This study aims to compare the field Glasgow Coma Score (fGCS) and the admission GCS (aGCS) as predictors of discharge status as measured by the Rancho Los Amigos (Rancho) score.

MATERIALS AND METHODS
This is a retrospective cohort study of blunt force TBI patients admitted directly to a Level 1 trauma center from 2007 to 2008. All data was identified within the TRACS database and the electronic medical record. All included patients had a field GCS score, an admission GCS score, and a Rancho score. Patients missing any score were excluded. Covariates examined as potential confounders were selected on the basis of clinical and statistical significance. Statistical analyses included ordinal logistic regressions and likelihood ratio tests.

CONCLUSIONS
Field GCS is the better predictor of short-term cognitive outcomes in the traumatic brain injury population. Obtaining an accurate fGCS score may improve disposition planning in patients with TBI.

ACKNOWLEDGEMENTS
Mario Davidson, PhD

MENTOR / DEPARTMENT
Dr. Melissa McPheeters Dr. Oscar D. Guillamondegui

SOCIAL SUPPORT AND MEDICATION ADHERENCE IN HOSPITALIZED PATIENTS

ABBY STUFFLEBAM MEYERS
HEALTHCARE AND PUBLIC HEALTH RESEARCH AND MANAGEMENT

BACKGROUND PROBLEM
To complement the expanding biomedical knowledge of disease, it has become increasingly clear that psychosocial factors play an equally important role in disease management and outcomes. Psychosocial factors, such as social support and depression, along with behavioral factors, such as medication adherence, are important determinants of hospitalizations. A better understanding of the prevalence of these factors, and their interrelatedness, could help providers prevent hospitalizations and better address these factors in discharge planning.

OBJECTIVES
The goal of this research was to characterize relationships between psychosocial characteristics - particularly demographics, cognition, numeracy, social support, and depression – and medication adherence.

MATERIALS AND METHODS
Inpatients at VUH were interviewed in a verbally-administered survey. Patients were selected from the daily census, and screened for eligibility and willingness to participate. Data from the interview responses were collected on a laptop and stored in REDCap. The validated instruments all sought patient-reported data, and included the Montreal Cognitive Assessment (MoCA), Subjective Numeracy Scale (SNS), the ENRICHD Social Support Inventory (ESSI), PHQ-9, and the Adherence to Refills and Medications Scale (ARMS). With SPSS, descriptive statistics were used to summarize patient characteristics, and to analyze relationships among variables using Pearson’s and Spearman’s correlation coefficients.

CONCLUSIONS
A significant relationship between
social support and medication adherence indicates the close ties between the psychosocial factors and behavior. This relationship should be further explored to assess for possible interventions that would allow providers to improve medication adherence and prevent unnecessary hospitalizations.

ACKNOWLEDGEMENTS
Sunil Kripalani, Courtney Cawthon, Ed Vasilevskis, Ken Wallston, Amanda Salanitro, Katharine Donato, and the rest of the VICS steering committee

MENTOR / DEPARTMENT
Sunil Kripalani, Department of Medicine
Experiences in the Laboratory Based Biomedical Research Area of the Emphasis Program are focused on hypothesis-driven investigation primarily based within a laboratory environment. Each student becomes an active participant in a research program and completes a clearly defined project. During the first year, the lab-based explorer becomes acclimated with new protocols, becomes an integral member of the team and becomes well versed in the foundational literature in his/her chosen field of focus. By summer the student is ready for full-time research making ever evolving modifications to the research plan while attending occasional relevant seminars with the cohort of students in the lab-based research area.

Guiding students as they move through the project selection phase with its wealth of potential mentors and research areas toward their transformation into skillful and meticulous contributors at the bench is rewarding and fascinating for Co-Directors Lillian Nanney, Ph.D. and Michael Laposata, MD, Ph.D. Some students select projects based on collection of human samples and subsequent analysis at the lab bench. Others select in vivo work with unique animal models. Still others conduct in vitro analysis using sophisticated molecular tools. As students immerse themselves in experiential learning, each begins to take ownership and pride in expected and unexpected accomplishments. By the end of second year most students are making plans for national poster presentations and several polish off portions of manuscripts. A select number of students develop a real affinity for lab-based investigation and quickly seek and find new mentors and projects and maintain a sustain research experience throughout medical school. A few become fully committed and plan for a Medical Scholars year or enter the MSTP program. Every student hones his/her abilities to critically evaluate journal articles. Each has an opportunity to improve their interpersonal skills while experiencing the synergistic power of collaborative research. All students come to realize that the thrill of success in lab research is balanced with formidable challenges. Each student develops a much richer appreciation for the behind-the-scenes effort and serendipity that fuels discoveries that shape the future of medicine.
A PRACTICAL COMPARISON OF NON-INVASIVE IMAGING TO CONVENTIONAL CATHETER ANGIOGRAPHY IN THE DIAGNOSIS OF CEREBRAL ANEURYSMS: A RETROSPECTIVE, SINGLE-CENTER ANALYSIS

NEIL BANSAL
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Based on numerous reports citing high sensitivity and specificity of non-invasive imaging (e.g. CTA or MRA) in the detection of intracranial aneurysms, it has become increasingly difficult to justify the role of conventional angiography (DSA) for diagnostic purposes. The current literature however largely fails to demonstrate the practical application of these technologies within the context of a “real-world” neurosurgical practice.

OBJECTIVES
We sought to determine the proportion of patients for whom the additional information gleaned from 3D rotational DSA (3DRA) led to a change in treatment.

MATERIALS AND METHODS
We analyzed the medical records of the last 361 consecutive patients referred to a neurosurgeon at our institution for evaluation of “possible intracranial aneurysm” or subarachnoid hemorrhage (SAH). Only those who underwent non-invasive vascular imaging within 3 months prior to DSA were included in the study. For asymptomatic patients without a history of SAH, aneurysms less than 5 mm were followed conservatively. Treatment was advocated for patients with unruptured aneurysms measuring 5 mm or larger and for aneurysms in the setting of acute SAH.

CONCLUSIONS
In a “real-world” analysis of intracranial aneurysms, DSA continues to play an important role in determining the optimal management strategy.

MENTOR / DEPARTMENT
Dr. Robert Mericle, Department of Neurosurgery

HELCOBACTER PYLORI TRXB AND CHEW MUTAGENESIS AFFECTS DIFFERENT MECHANISMS OF INFECTION AND GASTRIC INFLAMMATION

JOSHUA B. BILSBORROW
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Helicobacter pylori colonizes the gastric mucosa of approximately 50% of the global population. Chronic infection can lead to peptic ulcer disease, MALT lymphoma, or gastric adenocarcinoma in a small minority of individuals. The majority of H. pylori carriers never develop symptoms of infection, suggesting that host genetics and strain differences underlie epithelial damage and carcinogenesis.

OBJECTIVES
Proteomics comparisons between H. pylori 7.13 (a carcinogenic strain) and B128 (non-carcinogenic) demonstrated several genes that were differentially expressed in vitro. trxB, a thioredoxin reductase, was four times as abundant in strain 7.13 as compared to B128. Alternately, the chemotaxis protein cheW was about 1.25 times less abundant in 7.13. Deleting these genes from 7.13 would allow their specific roles in carcinogenesis to be clarified.

MATERIALS AND METHODS
trxB and cheW were amplified using PCR and mutated by the internal insertion of a kanamycin-resistance cassette. These altered versions were then re-introduced into H. pylori 7.13 and the mutants were screened for positive growth on kanamycin-containing medium.

CONCLUSIONS
Mutations in trxB were lethal, suggesting that the thioredoxin reductase gene is a requirement for growth under basic conditions. Increased expression of this protein in strain 7.13 compared to B128 may mediate carcinogenesis by providing the organism with a greater potential to withstand oxidative stresses induced by the host immune system. Preliminary results show that cheW mutants may not vary significantly from strain 7.13 in terms of infection phenotype, suggesting that this protein is not required for gastric colonization or that other chemotaxis genes might fulfill similar roles.

ACKNOWLEDGEMENTS
Dawn Israel, PhD Judith Romero-Gallo, PhD Jennifer Noto, PhD Niyomi Gandhi, BA

MENTOR / DEPARTMENT
Richard M. Peek, MD Director, Division of Gastroenterology, Hepatology, and Nutrition

A LOOK AT IN VIVO AND IN VITRO MODELS FOR MURINE ENDOCARDIOGENESIS

KEVIN CARR
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Endocardiogenesis, though a vital component of cardiogenic development in mammalian models has yet to be completely understood. This is an integral developmental stage in mammalian cardiogenesis in which developmental anomalies have been implicated in severe congenital valvular abnormalities, via its association with epithelial to mesenchyme transformation that characterizes the initiation and subsequent modeling of cardiac valves. An understanding of the intricacies of this developmental process will not only provide insight into the embryologic origin of these anatomical malformations, but will also fortify us with the knowledge on how to possibly intervene embryologically to stave the progression of such diseases.
To this end there still is not a suitable study model that can accurately recapitulate the development of the endocardium.

**OBJECTIVES**
We have designed an in vivo model utilizing the previously described nFATc1 gene as a marker for endocardial development. Engineering a transgenic mouse with fluorescently labeled nFATc1, we aim to demonstrate that we can now chronologically recapitulate endocardial development in vivo, and utilize this model to generate an in vitro model that accurately recapitulates these developmental stages.

**MATERIALS AND METHODS**
In order to gauge in vivo, the development of the endocardium, transgenic mice were created using an nFATc1-mCherry BAC transgene. The BAC transgene also contained a nuc-cerulean nFATc1 fluorescent tag, conjugated to the histone h2b protein. The animals were maintained as per protocols approved by the Vanderbilt University Institutional Animal Care and Use Committee (IACUC). Animals were harvested at daily intervals from E7.5 until E12.5 in order to be studied. Whole embryos were surgically excised and analyzed via fluorescence microscopy using a Nikon Eclipse E800. For sectional analysis, embryos were sectioned at 10um thickness and mounted with VectaShield media containing DAPI, and viewed using a Zeiss Upright LSM510 confocal microscope.

**CONCLUSIONS**
From fluorescence analysis, we notice a continued expression of nfatc1 throughout the heart even at day 12.5 of development. These results conflict with previously shown data that alludes to a decrease in expression in all areas of the endocardium, excepting the regions not undergoing epithelial to mesenchyme transformation (EMT). Theoretically, this may be due to incomplete recapitulation of the in vivo development through the use of our transgenic mice. Due to the structure of the nFATc1-mCherry gene product incorporating the fluorescent dye in the cell membrane via a glycosylphosphatidylinositol (Gpi) tag, there may not be congruency between the wild type and model protein turnover rates, and as such the fluorescence remains present longer than what is represented in vivo. This may or may not be the case for the histone h2b conjugated cerulean tag. Thus more work needs to be done in understanding how to accurately recapitulate these developmental processes.

**MENTOR / DEPARTMENT**
Scott Baldwin, Developmental Biology T35 NIH Grant, Summer Research Training Program in Heart, Lung and Vascular Biology

**HIGH FAT DIET INCREASES APOPTOSIS WITHIN CROWN-LIKE-STRUCTURES IN MICE ADIPOSE TISSUE**

**JASON CHEN**
LABORATORY-BASED BIOMEDICAL RESEARCH

**BACKGROUND PROBLEM**
The adipose tissue (AT) of obese individuals is known to exist in a chronic inflammatory state, believed to contribute to insulin resistance and diabetes. Many studies have associated the inflammation with an increase in adipose tissue macrophages (ATMs) and their polarization into an inflammatory phenotype. It is hypothesized that as adipocytes outgrow their local blood supply during obesity and become necrotic, the release of free fatty acids (FFAs) and specific factors leads to the recruitment of macrophages to surround adipocytes in the form of crown-like-structures (CLSs) in order to phagocytose the dead adipocytes. Using a cell culture model, our lab has shown that excess intracellular accumulation of free fatty acids induces inflammation, lipotoxicity, and apoptosis in macrophages.

**OBJECTIVES**
The goal of my study was to determine whether exposure of ATMs to fatty acids induces apoptosis in vivo.

**MATERIALS AND METHODS**
The white adipose tissue of mice fed a 10%, 45%, or 60% saturated fat diet were embedded in paraffin, sectioned, and then stained with toluidine blue to count total CLSs, cleaved caspase 3 antibody to count number of apoptotic cells and F4/80 antibody to count number of macrophages. Images and counts were obtained using Histometrix program.

**CONCLUSIONS**
Further studies into the fate of the apoptotic cells are warranted to examine the fate of the apoptotic macrophages to understand their effect on inflammation. Under acute inflammation, resolution of inflammation occurs by the phagocytosis of apoptotic immune cells, a process known as efferocytosis. It may be that during chronic inflammation, impaired efferocytosis prolongs or enhances inflammation.

**MENTOR / DEPARTMENT**
Alyssa Hasty, Department of Molecular Physiology & Biology, Vanderbilt University, Nashville, TN

**DETERMINING KCNQ1 ALLELIC IMBALANCE IN HUMAN HEART**

**TYFFANY CHEN**
LABORATORY-BASED BIOMEDICAL RESEARCH

**BACKGROUND PROBLEM**
The voltage-gated potassium channel Kv7.1 is encoded by the gene KCNQ1 and is essential for the repolarization phase of the cardiac action potential. KCNQ1 mutations are a common cause of congenital long QT syndrome (LQTS), a genetic disorder characterized by electrocardiogram abnormalities that heralds a predisposition to syncope, seizures, and sudden cardiac death at a young age due to cardiac arrhythmia. The prevalence of LQTS is estimated to be 1 in 2500.
OBJECTIVES
KCNQ1 is an imprinted gene that exhibits strong monoallelic expression in many tissues except heart. However, studies have detected an imbalance in cardiac maternal-paternal allelic expression that may suggest some level of imprinting. We hypothesize that KCNQ1 expression is not simply biallelic in adult heart tissue, but rather exhibits varying levels of imprinting. This relaxation in imprinting may explain the variable penetrance of LQTS in some families.

MATERIALS AND METHODS
Next-generation sequencing was used to investigate cardiac imprinting of KCNQ1. RNA was extracted from 110 adult heart tissue samples obtained from relatively healthy adults aged 16-65. RNA was reverse transcribed to cDNA to enable genotyping of a common KCNQ1 variant for use in tracking separate parental alleles. Twenty-eight samples that were heterozygous for the common variant were submitted for quantitative analysis using next-generation 454 pyrosequencing to determine the percentage of allelic expression. As a control experiment, RNA from lymphoblastoid cell lines known to exhibit strong KCNQ1 imprinting were assayed in parallel.

CONCLUSIONS
Data collected in this study may have important implications in the diagnosis and treatment regimen of individuals affected by or at risk for LQTS. This study may improve the accuracy of familial genetic testing and prevent incidence of fatal cardiac events.

ACKNOWLEDGEMENTS
Christine Simmons

MENTOR / DEPARTMENT
Dr. Al George Genetics Medicine

CORDOTOMY VERSUS LARYNGEAL PACING FOR BILATERAL VOCAL FOLD PARALYSIS

JENNIFER DANG
and wildtype (N2) nematodes were challenged with 0-50µM MeHg for 30 minutes. Live nematodes were counted in adult stages to evaluate lethality. Imaging studies were also performed at L4 and adult life stages to assess dopaminergic neurons after MeHg challenge.

CONCLUSIONS
Our data suggest C. elegans is a valuable model for studying the effects of MeHg on the nervous system, delineating molecular mechanisms of toxicity and determining genetic susceptibility. Based on lethality studies, skn-1 is protective against MeHg toxicity.

MENTOR / DEPARTMENT
Ebany Martínez-Finley Michael Aschner Vanderbilt Division of Pediatric Toxicology and Center in Molecular Toxicology

INVESTIGATION OF EARLY OPTIC NERVE DAMAGE DUE TO INTERMITTENT ELEVATED IOP
ERIN C. FULCHIERO
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Glaucoma with destruction of retinal ganglion cells is a leading cause of irreversible worldwide blindness. The earliest pathological changes in glaucoma are not well understood. Peroxynitrite-mediated oxidative injury has been reported in human glaucoma blood vessels.

OBJECTIVES
In the current study, we evaluate whether evidence of peroxynitrite-mediated oxidative injury is present within the eye following early IOP elevation.

MATERIALS AND METHODS
IOP was transiently elevated for 1 hour with an adjustable lasso around the right topically anesthetized eye of Sprague-Dawley rats. IOP was measured before, immediately after, at the end of 1 hour treatment, and 1 hour after rest using TonoLab tonometry (Tiolat Oy [Helsinki, Finland]). Following perfusion, sagittal sections were prepared for immunohistochemistry with antibody to nitrotyrosine (Cell Signaling Technology). Intensity of immunoreactivity was assessed semi-quantitatively using the MetaMorph® Microscopy Automation & Image Analysis Software.

CONCLUSIONS
One hour of moderate elevation in intraocular pressure increased nitrotyrosine immunohistochemical staining within the pre-laminar optic nerve vessels in our rat model. This is consistent with changes seen in chronic human glaucoma tissue.

ACKNOWLEDGEMENTS
Ratna Prasad, Ph.D.; Pengchung Lu, M.S; Bob Matthews, Ph.D.; Sean Shaffer; Sam Wells, Ph.D.; Carol Bonner

MENTOR / DEPARTMENT
Karen M. Joos, M.D., Ph.D. in Ophthalmology

ALDH7A1 EXPRESSION IS ASSOCIATED WITH RECURRENCE IN PATIENTS WITH RESECTED NSCLC
NICHOLAS J. GIACALONE
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
The aldehyde dehydrogenase (ALDH) enzymes are important for detoxification of endogenous and exogenous aldehydes. Expression of ALDH family members has recently been described as a potential marker for tumor-initiating cancer stem cells in a variety of human malignancies, including lung cancer.

OBJECTIVES
We were interested to determine whether expression of ALDH7A1, a member of the ALDH family, has prognostic significance in resected non-small cell lung carcinoma (NSCLC).

MATERIALS AND METHODS
Tumor specimens were obtained for 107 patients with completely resected stage I through stage III NSCLC from paraffin-embedded tissue microarrays and stained with an antibody specific for ALDH7A1. Staining patterns were graded by a pathologist based on the intensity of staining and the percentage of cells stained. A staining score index was calculated by multiplying intensity score by the percentage area with positive staining.

CONCLUSIONS
These data indicate that ALDH7A1 staining is present in a substantial number of NSCLC tumors and may be a biomarker predictive for increased incidence of cancer recurrence in patients with surgically resected NSCLC.

ACKNOWLEDGEMENTS
Rosana Eisenberg, MD, Heidi Chen, PhD, Sandra Olsen, MS, Pierre Massion, MD, David Carbone, MD, PhD; Financial Support: NIH/NCRR: Vanderbilt CTSA Grant UL1 RR024975 (PI: Nicholas J Giacalone); NIH: T35 ES016534 (PI: Peter Guengerich, PhD)

MENTOR / DEPARTMENT
Bo Lu, MD, PhD, Department of Radiation Oncology

EFFECT OF ESTROGEN METABOLITES ON BMPR2 EXPRESSION AND PULMONARY ARTERIAL HYPERTENSION
EVERETT GU
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Hereditary pulmonary arterial hypertension is an autosomal dominant disease caused by mutations in bone morphogenic protein receptor type 2 (BMPR2) gene in 80-85% of cases. One of the most intriguing features of this disease is that women with BMPR2 mutations are 2-fold more likely...
to develop disease than men, but the molecular mechanisms for this remain unclear. Our data show that functions of genes critical to estrogen metabolism are upregulated in females compared to males, implying that increased estrogen activity might increase PAH risk.

OBJECTIVES
To test the hypothesis that estrogen and its metabolites directly affect pulmonary microvascular endothelial cell (PMVEC) function by regulating BMPR2 expression.

MATERIALS AND METHODS
PMVECs were cultured and exposed to one of five different sex hormones at variable concentrations: estrone (E1), 17β-estradiol (E2), estriol (E3), 16α-hydroxyestrone (16α-OHE), and testosterone. An in vitro scratch assay was performed to quantify the proliferation rate: a confluent cell monolayer was scratched and exposed to a single sex hormone over a period of time. Real-time polymerase chain reaction (RT-PCR) was performed to quantify the mRNA levels of BMPR2 after exposure of cells to a single sex hormone for a set time period.

CONCLUSIONS
Exposure of PMVECs to different sex hormones at different concentrations influences their proliferation rate and their level of expression of BMPR2, but the exact relationship between BMPR2 expression and proliferation rate has yet to be defined.

MENTOR / DEPARTMENT
Rizwan Hamid, MD, PhD and Eric Austin, MD, MSci

RICTOR, THE BRAIN, AND OBESITY
SCOTT HAGAN
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Energy homeostasis is tightly regulated by an endocrine feedback loop in which insulin and leptin target hypothalamic neurons that express NPY/AgRP and POMC to modulate energy balance. Rictor, when in association with the mTORC2 complex, phosphorylates Akt and may be important for insulin and leptin signaling through the PI3K-Akt pathway in neurons.

OBJECTIVES
Our hypothesis that Rictor is a key determinant of neuronal insulin and leptin responsiveness, and that deletion of Rictor in AgRP and POMC neurons will lead to an exaggerated glucose intolerance and obesity phenotype, respectively, in mice on a low-fat diet.

MATERIALS AND METHODS
To test this hypothesis, we used Cre-LoxP recombination to develop neuronal knockouts of Rictor in mice lines. Using a Nestin-Cre driver, we first accomplished a total brain knockout of Rictor, and subjected animals to a Chow diet for 25 weeks. We then subjected AgRP and POMC neuron-specific knockouts of Rictor to a Chow diet for 25 weeks.

CONCLUSIONS
The mice studies suggest that Rictor action in POMC and AgRP-expressing neurons may be critical for energy balance. Larger cohorts of POMC and AgRP-specific Rictor knockout mice subjected to high fat diets will be studied to expose more clearly potential obesity and glucose metabolism phenotypes.

ACKNOWLEDGEMENTS
Heidi Kocalis, Leena George, Kelly Rogers, Maxine Turney, Richard Printz

MENTOR / DEPARTMENT
Kevin Niswender, Department of Medicine in the Division of Diabetes, Endocrinology and Metabolism

THE ROLE OF FOXM1 IN GROWTH FACTOR MEDIATED β-CELL PROLIFERATION
AMANDA HARRIS
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
The FoxM1 transcription factor is expressed in proliferating cells and is critical for cell cycle progression. In the pancreas, FoxM1 regulates postnatal β cell expansion. Despite the knowledge that FoxM1 is activated by proliferative stimuli, little is known about the signaling pathway(s) responsible in β cells.

OBJECTIVES
We hypothesize that FoxM1 operates downstream of various growth factors and is a nexus for different mitogenic signals.

MATERIALS AND METHODS
We examined the effect of Placental Lactogen (PL), a β cell mitogen, on Foxm1 mRNA expression in islets and also how second messenger pathway inhibitors affect PL-induced Foxm1 expression. To identify the upstream PL-responsive regulatory regions, we transfected a Foxm1 promoter-Luciferase reporter gene into immortalized β cells. To determine whether Foxm1 expression correlates with responsiveness of aging β cells to mitogenic stimuli, we examined baseline and PL-induced Foxm1 expression in islets from different aged mice. Finally, we compared Foxm1 expression in human islets from Type II diabetics and non-diabetics.

CONCLUSIONS
It appears FoxM1 is a target of many mitogenic signals in β cells and that the ability of these signals to induce Foxm1 expression decreases with age. Thus, restoration of FoxM1 expression and activity in older islets may improve beta cell mass.

MENTOR / DEPARTMENT
Maureen Gannon, Molecular Physiology & Biophysics
PHASE SPACE PLOTS AND CORRELATION DIMENSION ANALYSES OF ELICITED MODAL, RAISED, AND PRESSED RABBIT PHONATION

LAURENCE JAMES
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Rousseau et al. have developed an in vivo method for eliciting vocalization from rabbits in order to better understand the effects of phonation on the development of vocal fold pathology. Using this model, our laboratory has successfully demonstrated the ability to elicit three distinct phonation types namely modal, raised intensity, and pressed from rabbits. Methods for reliably analyzing these complex signals are needed in order to understand differences between these various phonation types.

OBJECTIVES
The purpose of the present study was to evaluate the usefulness of non linear dynamic analysis to characterize modal, raised, and pressed phonation in an evoked rabbit phonation model.

MATERIALS AND METHODS
Seventeen New Zealand white breeder rabbits (3 to 5kg) were used to perform the study. Acoustic signals were recorded using a dynamic microphone placed 10 cm from the opening of the laryngoscope and digitized using the Computerized Speech Lab Software. Central portions of the acoustic waveform for modal, raised, and pressed phonations were analyzed via phase space plots and the estimation of the correlation dimension (D2).

CONCLUSIONS
Our analysis has given us an improved understanding of standardizing phonation dose and the underlying conditions that may affect the complexity of vibration in different modes of phonation. This will allow us to gain valuable insight in to future biochemical experiments using our model.

ACKNOWLEDGEMENTS
Dr. Shaheen Awan Ph.D
Department of Audiology and Speech Pathology, Bloomsburg University
MENTOR / DEPARTMENT
Bernard Rousseau, Department of Otolaryngology, Vanderbilt University

HEAT KILLED STAPHYLOCOCCUS AUREUS INDUCE A PROCOAGULANT PHENOTYPE ON CULTURED HUMAN ENDOTHELIAL CELLS

WESTON LANGDON
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Deep venous thrombosis is rare in children but occurs in ten percent of pediatric cases of acute hematogenous osteomyelitis. Presence of deep venous thrombosis is associated with severe onset, extensive local disease as well as septic emboli leading to lung infiltrates. The common strain of community-acquired, methicillin-resistant Staphylococcus aureus (USA-300) may have a higher likelihood of causing deep venous thromboses than strains of methicillin-susceptible Staphylococcus aureus. Elucidating the effects of Staphylococcus aureus on the procoagulant state of cultured endothelial cells can give insight on the pathogenesis of pediatric deep venous thromboses.

OBJECTIVES
Quantify the difference in thrombin generation from cultured endothelial cells exposed to heat killed methicillin-resistant Staphylococcus aureus to cells without bacterial exposure.

MATERIALS AND METHODS
A novel thrombin generation assay was used to measure thrombin generated from endothelial cells exposed to human plasma.

CONCLUSIONS
Methicillin-resistant Staphylococcus aureus induce expression of tissue factor when cultured with endothelial cells which leads to higher thrombin generation. Direct activation of endothelial cells may play a role in the pathogenesis of deep venous thrombosis associated with osteomyelitis.

ACKNOWLEDGEMENTS
Buddy Creech MD, Elizabeth Saye, Nicholas Mignemi, Lynda O’Rear, Jiro Ichikawa MD, Baldeep Pabla, Maria Tamborski

MENTOR / DEPARTMENT
Jonathan Schoenecker MD, PhD, Department of Orthopaedics, Department of Pediatrics, Department of Pharmacology

STRETCHED-INDUCED ACTIVATION OF P2X7 RECEPTORS IN SAPHEOUS VEINS

OPAL LIN-TSAI
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
The leading cause of failure of coronary and peripheral revascularization procedures is intimal hyperplasia, a complex process thought to be triggered by vein graft injury during harvest. Injurious techniques include mechanical stretching and the use of saline and surgical skin markers.
Stretching is thought to release ATP, which activates the purinergic P2X7 receptors and apoptotic caspase cascades.

**OBJECTIVES**
Our laboratory identified a blue food dye (BD) as a non-toxic marker that also restores functional viability to injured saphenous veins. This study sought to determine a potential P2X7 receptor antagonism by BD during stretch-induced injury.

**MATERIALS AND METHODS**
Porcine saphenous vein (PSV) was pretreated with BD prior to treatment with BzATP, a stable analogue of ATP, and contractile responses were measured in a muscle bath. In another experiment, caspase-3 activation was assessed in rat aorta that were mechanically stretched or treated with BzATP. Similar experiments were also performed with cultured smooth muscle cells.

**CONCLUSIONS**
Our results suggest that BD restores stretch injury through P2X7 receptor antagonism, leading to blockade of downstream apoptotic responses. Accordingly, BD is a non-toxic alternative to surgical skin markers for vein marking and serves as a potential therapeutic in preventing vein graft injury during harvest.

**ACKNOWLEDGEMENTS**
Kyle Hocking; Padmini Komalavilas; Joyce Cheung-Flynn

**MENTOR / DEPARTMENT**
Colleen Brophy, Department of Surgery

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**EXAMINING THE ROLE OF APOPTOSIS AND IMMUNE ACTIVATION IN HIV INFECTION**

**RISHI D. NAIK**

**LABORATORY-BASED BIOMEDICAL RESEARCH**

**BACKGROUND PROBLEM**
Though the rate of CD4+ T cell decline is linked to the level of HIV viremia, HIV-infected subjects show evidence of generalized immune activation that is independently associated with HIV disease progression. T cells from HIV-infected individuals also show enhanced susceptibility to apoptosis. One major apoptotic pathway is triggered after mitochondrial membrane permeabilization; however, the role of mitochondrial dysfunction, and its relation to CD4+ T cell decline after HIV infection is unclear.

**OBJECTIVES**
Our goal is to determine the relationship between mitochondrial mass within T lymphocytes, and levels of immune activation and apoptosis in HIV-infected individuals with a wide range of CD4+ T cell counts and viral loads.

**MATERIALS AND METHODS**
T cells were analyzed by flow cytometry for apoptosis (Annexin V), mitochondrial mass (Mitotracker Green) and immune activation (CD38 expression). For standardization of the anti-CD38 and MT green stains, frozen peripheral blood mononuclear cells from a healthy control was used in every experiment.

**CONCLUSIONS**
Overall our data show that CD8+ and CD4+ T cells are selectively characterized by increased Mitochondrial Mass and immune activation of early apoptotic cells, when compared to non-apoptotic cells. We will sequence the mitochondrial genomes of this cohort of infected individuals to determine whether particular mitochondrial sequences are associated with increased levels of mitochondrial dysfunction in HIV infection.

**ACKNOWLEDGEMENTS**
I would especially like to thank my mentor, Dr. Spyros Kalams, for his guidance, support, and dedication. I would also like to thank Louise Barnett, Emily Zern, Rita Smith, and other members of the Kalams lab group for assistance on this project. Finally, I want to thank Dr. Nanney and the Emphasis Program for their assistance.

**MENTOR / DEPARTMENT**
Dr. Spyros Kalams, Division of Infectious Diseases, Department of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee, United States of America
HCC193 and H460 cells in vitro. More research is warranted to test the mechanism of action of BV6, and to assess its potential in vivo and in the clinical setting.

**MENTOR / DEPARTMENT**
Dr. Bo Li, Department of Radiation Oncology

**APPLICATIONS OF A CELLULAR THROMBIN GENERATION ASSAY**
BALDEEP S. PABLA
LABORATORY-BASED BIOMEDICAL RESEARCH

**BACKGROUND PROBLEM**
Whereas current clinical tests of coagulation focus on the contribution from the extrinsic and intrinsic clotting cascades, thrombin generation measuring techniques have emerged as a method of measuring the overall state of coagulation in a given biological system by measuring the output of the competing forces that characterize the coagulation systems. While it is known that tissue factor is up regulated in many cancers, the characterization of how expression of this surface protein along with the expression of other proteins central to the coagulation cascade work to produce the net pro-thrombotic phenotype observed in cancer has not been reported.

**OBJECTIVES**
Here, an attempt was made to produce a reproducible cell based thrombin generation assay that allowed the characterization various cell lines on the basis of their thrombin generation profile.

**MATERIALS AND METHODS**
Specifically, BxPC-3 (pancreatic adenocarcinoma), MDAMB231 (aggressive breast adenocarcinoma) and MCF7 (less aggressive breast adenocarcinoma - control) were analyzed on cellular based thrombin generation assay using both factor eight deficient plasma (FVIIIID) and complete plasma to further elucidate the nature of the hypercoagulable state observed in vivo with these cancerous cells.

**CONCLUSIONS**
The hypercoagulable state of cells can be well characterized by using cellular thrombin generation techniques. The clinical applicability of this assay is vast and with more continued research, could greatly improve the precision with which with anticoagulate patients with hypercoagulable states.

**ACKNOWLEDGEMENTS**
I would like to thank Dr. Nipun Merchant and Dr. Nagaraj Nagathihalli of Merchant Lab (Division of Surgical Oncology, VUMC) for their assistance in obtaining and maintaining the BxPC3 cell line. I’d like to thank Dr. Jiro Ichikawa, MD, PhD, Lynda O’Rear, Nicholas Mignemi and Weston Langdon for their technical support in helping to obtain data for this project. I’d like to thank Dr. Jonathan Schoenecker for his guidance and support throughout the summer.

**MENTOR / DEPARTMENT**
Dr. Jonathan Schoenecker, Department of Orthopaedics.

**RETROCOCHLEAR PATHOLOGY AND ASYMMETRIC HEARING LOSS: A COST BENEFIT ANALYSIS OF A DIAGNOSTIC TOOL**
KLINT PEEBLES
LABORATORY-BASED BIOMEDICAL RESEARCH

**BACKGROUND PROBLEM**
Asymmetric sensorineural hearing loss (ASNHL) is estimated to occur in up to 50% of patients seen by otolaryngologists and is a presentation in which retrocochlear tumors must be ruled out as the underlying etiology. Currently, MRI is the modality with the best positive predictive value, resulting in a significant cost to the health care system as only a minority of ASNHL patients have tumors.

**OBJECTIVES**
To determine the probability of a retrocochlear pathologic diagnosis given an initial presentation of asymmetric hearing loss and to establish the cost to the healthcare system of each positive MRI.

**MATERIALS AND METHODS**
Retrospective chart review of all patients under four specific providers in the VUMC otolaryngology practice with a history of ASNHL from June 2001 to July 2010 using the search term ‘asymmetric.’

**CONCLUSIONS**
As the cost of a typical MRI study to investigate retrocochlear pathology in ASNHL patients is substantial ($45,339.14 for each tumor diagnosed by MRI), and a positive study occurs in only 1.98% of all initially unknown etiology ASNHL patients, it would be advantageous to develop a more cost-effective diagnostic modality (other imaging, laboratory, etc.) that retains the high positive predictive value of MRI.

**MENTOR / DEPARTMENT**
Robert F. Labadie, MD PhD, Department of Otolaryngology Ted McRackan, MD, Department of Otolaryngology, PGY3

**CFTR DYSFUNCTION IS IMPLICATED IN ALTERED EXPRESSION OF ENZYMES INVOLVED IN FATTY ACID METABOLISM**
SARAH PROFFITT
LABORATORY-BASED BIOMEDICAL RESEARCH

**BACKGROUND PROBLEM**
Cystic fibrosis (CF) is a monogenetic disease caused by mutations in the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) and typically
involves recurrent pulmonary infections associated with excessive inflammation. Specific fatty acid alterations have been described in CFTR-expressing tissue in CF patients, including decreased levels of linoleic acid (LA) and increased levels of its downstream metabolite, arachidonic acid (AA). AA serves as the precursor of eicosanoids, which are potent inflammatory mediators. Thus, altered fatty acid levels may play an important role in the excessive airway inflammation observed in CF patients, though the mechanisms by which mutations in CFTR lead to such alterations remain unclear.

**OBJECTIVES**

Using human bronchial epithelial (HBE) cells, we investigated the connection between CFTR-mediated chloride conductance and the expression of FADS1 and FADS2, genes that encode desaturase enzymes involved in the metabolism of LA to AA.

**MATERIALS AND METHODS**

Gene expression was evaluated in three groups of cells: HBE cells expressing CFTR (“sense cells”), HBE cells expressing CFTR that were treated with an inhibitor of CFTR-mediated chloride transport, and HBE cells transfected with an antisense RNA such that they do not express CFTR (“antisense cells”). mRNA was harvested following Trizol reagent protocol and levels of transcripts encoding fatty acid metabolic enzymes were measured using qRT-PCR.

**CONCLUSIONS**

These findings indicate that sense cells treated with CFTR inhibitor exhibit similar patterns of FADS1 and FADS2 gene expression as antisense cells. This suggests that CFTR-mediated chloride conductance plays a direct role in the regulation of fatty acid metabolism and that CFTR dysfunction may be responsible for the specific fatty acid alterations observed in CF.

**MATERIALS AND METHODS**

Paw edema is induced in rats by injecting carrageenan solution in the foot pad. Pilot studies were conducted to determine the edema time-curve after carrageenan injection and determine the ideal scavenger injection time. Scavengers were tested at decreasing doses intraperitoneally, and will then be tested orally. Paw volume was measured over time to determine reduction in inflammation. Paws will be collected for quantitative analysis of y-ketoaldehyde-protein adducts.

**CONCLUSIONS**

γ-ketoaldehyde scavengers seem to have a greater ability to reduce inflammation than current COX inhibitors. Future analysis will give us insight into the molecular effects of scavengers as well as determine which scavengers have oral efficacy, which could assist in future drug design.

**ACKNOWLEDGEMENTS**

Brooke Pantazides, Bill Zackert

**MENTOR / DEPARTMENT**

L. Jackson Roberts, II, MD, Clinical Pharmacology

**ROLE OF MECHANICAL STRETCHING IN TIE1 EXPRESSION AND GENE REGULATION IN THE FORMATION OFATHEROSCLEROTIC PLAQUES**

**LARA SELTZ**

**LABORATORY-BASED BIOMEDICAL RESEARCH**

**BACKGROUND PROBLEM**

Tie1 and Tie2 comprise a unique class of endothelial receptor tyrosine kinases that serve a functional role in vascular stabilization and disease states, such as atherosclerosis. Our group has recently shown that atherogenic, turbulent flow upregulates Tie1 expression in endothelial cells both in vitro and in vivo. Furthermore, attenuation of Tie1 decreases atherosclerotic burden. While it has been suggested that mechanical stress, resulting
from radial stretch, also induces upregulation of Tie1 during vascular remodeling in coronary vascular endothelial cells in vitro, the effect of stretch on Tie1 expression in atherosclerotic prone aortic endothelial cells has not been previously evaluated.

OBJECTIVES
The aim of this study was to delineate the effect of mechanical stretch on Tie1 expression and gene regulation in vitro in mouse aortic endothelial cells (MAEC). The first objective was to quantify changes in Tie1 expression in response to cyclic stretch. The second objective was to determine the effect of Tie1 attenuation on stretch induced gene regulation.

MATERIALS AND METHODS
Changes in Tie1 transcription and protein expression levels were examined in Immortalized Mouse Aortic Endothelial Cell (ImoMAEC) and Tie1lox/lox:SCL-ERT-Cre Immorto MAEC. MAECs were cyclically stretched at 1 Hz to 10% for 24 hours using the Flexcell FX-5000 Tension System. Tie1 RNA and protein expression were assessed by real-time PCR and western blot analysis.

CONCLUSIONS
Pending results from studies optimizing PCR analysis will further delineate the relationship between mechanical stretch in athrogenic regions of the adult vasculature and Tie1 expression. In the future, a candidate gene approach using targeted PCR array will be used to evaluate the effect of Tie1 attenuation on genetic regulation of inflammatory and angiogenic pathways.

ACKNOWLEDGEMENTS
Kel Vin Woo, Ph.D., Chris Brown, Ph.D., and NIH T-35 SRTP Research Program.

MENTOR / DEPARTMENT
H. Scott Baldwin, M.D., Cell and Developmental Biology

EXPLORING POTENTIAL INTERVENTIONS FOR ANGELMAN SYNDROME USING A MOUSE MODEL

LAKSHMI SIVARAJAN

LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Angelman syndrome (AS) is a neurogenetic disorder caused by deletion or mutation of the maternally imprinted gene UBE3A located at 15q11-13. Clinically, the disorder is characterized by movement and gait disturbances, developmental delay, and early-onset epilepsy with characteristic EEG abnormalities. Angelman syndrome individuals also frequently exhibit a characteristic EEG pattern and both partial and generalized seizure types. While seizures may be refractory, many Angelman syndrome patients respond to low doses of benzodiazepines and do not typically develop tolerance that limits the chronic use of this class of antiepileptic medications in most epilepsy patients.

OBJECTIVES
We chose to compare the effect of benzodiazepine treatment in wild-type and Ube3a knockout mice on multiple behavioral measures where the knockout mice have an abnormal phenotype. The behavioral experiments of interest were open field testing, acoustic startle and pre-pulse inhibition, and rotorod.

MATERIALS AND METHODS
Seventy-six mice were treated and tested over three cohorts in this experiment. The mice were of the C57/Bl-6 strain, and were bred to be maternally imprinted gene UBE3A allele. The mice were injected intraperitoneally twice daily with either saline solution or 0.13 mg/kg of clonazepam for six days prior to and including the experimental period (4 days) during which behavioral tests were conducted. This dosage was chosen as it was consistent with benzodiazepine dosages reported in the literature. Behavioral tests that were conducted include open field, acoustic startle reflex and pre-pulse inhibition, and rotorod.

CONCLUSIONS
From the data we acquired, we believe that the trends suggest that clonazepam appears to favorably impact behavioral outcomes of maternal Ube3a knockout mice. We hypothesize the dose to have been insufficient to generate significant differences between the trial and placebo arms. We plan to repeat the treatment using a two to three-fold increase in clonazepam dosage and re-evaluate the outcomes of the open field, acoustic startle and pre-pulse inhibition.

ACKNOWLEDGEMENTS
Terry Jo Bichell, Lisa Herrington, Rahul Jawa, Yueli Zhang

MENTOR / DEPARTMENT
Kevin F. Haas M.D. Ph. D. (Neurology, Epilepsy Division)

GLUCAGON-LIKE PEPTIDE-1 PROMOTES BETA CELL PROLIFERATION & IMPROVES GLYCEMIC CONTROL IN A MURINE MODEL OF NEONATAL DIABETES

MICHAEL A. SPINNER

LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Glucagon-like peptide-1 (GLP-1) has been shown to potentiate insulin secretion, promote beta cell proliferation, and reduce apoptosis.

OBJECTIVES
To test the hypothesis that GLP-1 would preserve beta cell function and improve glycemic control in a murine model of neonatal diabetes, we examined the effects of a GLP-1 agonist (exendin-4) on Akita mice, which are characterized by severe and progressive hyperglycemia.

MATERIALS AND METHODS
Upon weaning, wild type and
Akita littermates were given daily intraperitoneal injections of exendin-4 or PBS for a four-week period. Random blood glucose (BG) was measured twice per week, and fasting BG, plasma insulin, and plasma glucagon were measured at the end of the treatment period following a six-hour fast. In pancreatic cryosections, beta cell proliferation was assessed by Ki67 labeling and apoptosis by TUNEL staining.

**CONCLUSIONS**

The initial reduction in BG and the maintenance of reduced BG levels suggest both an acute and chronic effect of GLP-1 in improving glycemic control, including acute stimulation of insulin secretion and stimulation of beta cell proliferation. These findings suggest some therapeutic benefit of a GLP-1 agonist in preserving beta cell function and reducing hyperglycemia in neonatal diabetes.

**ACKNOWLEDGEMENTS**

Greg Poffenberger, lab manager

**MENTOR / DEPARTMENT**

Ioannis G. Papagiannis, Chunhua Dai, and Alvin C. Powers Department of Medicine: Division of Diabetes, Endocrinology, and Metabolism

**STUDYING METABOLIC SYNDROME IN MOUSE MODEL OF LUPUS**

**AUDREY YE**

**LABORATORY-BASED BIOMEDICAL RESEARCH**

**BACKGROUND PROBLEM**

We recently identified ADAMTS10 as a candidate glaucoma gene in the Beagle model of inherited primary open-angle glaucoma (POAG).

**OBJECTIVES**

The purpose of this study is to investigate the association of ADAMTS10 with human glaucoma.

**MATERIALS AND METHODS**

Patients with open-angle glaucoma were identified for screening of the exon and exon/intron junction regions of ADAMTS10. These patients include 12 primary congenital glaucoma (PCG), 16 juvenile open-angle glaucoma (JOAG), 3 adult-onset POAG, 15 pseudoexfoliation glaucoma (PEXG) and 18 pigment-dispersion glaucoma (PDG) patients. Nineteen cataract control patients (CC) without glaucoma were also included in the pilot cohort. Sequencing results were analyzed with Sequencher 4.9. Novel non-synonymous (NS) variants were confirmed with either restriction digests and/or resequencing.

**CONCLUSIONS**

Sequencing ADAMTS10 in patients with various types of open-angle glaucoma revealed 2 novel NS SNPs and 1 novel int/ex junction SNP not present in control patients. These 3 variants are potential candidates for glaucoma-associated mutations in ADAMTS10 in human glaucoma. Further screening of 79 additional adult-onset POAG patients is underway.

**ACKNOWLEDGEMENTS**

Research to Prevent Blindness, Inc., American Glaucoma Society MAPS Grant, NIH Grants R01EY020894, EY018435, P30-EY008126

**MENTOR / DEPARTMENT**

John Kuchtey, Ph.D., Rachel W. Kuchtey, M.D., Ph.D., Department of Ophthalmology

**STUDYING METABOLIC SYNDROME IN MOUSE MODEL OF LUPUS**

**AUDREY YE**

**LABORATORY-BASED BIOMEDICAL RESEARCH**

**BACKGROUND PROBLEM**

Systemic lupus erythematosus (SLE) is often known as an autoimmune disorder characterized by widespread inflammation and immune complex deposition in key target organs. Less well known is that SLE patients have greater incidence of metabolic syndrome, but the exact mechanism of this phenomenon is unclear. Past research has demonstrated a connection between autoimmunity and insulin resistance.

**OBJECTIVES**

To study the mechanism of insulin resistance and adipose tissue remodeling in relation to inflammation and autoimmunity.

**MATERIALS AND METHODS**

Experiments were carried out in B6.Sle 1.2.3 mice, which are triple congenic mice that express a lupus phenotype similar to that of humans. They were given high fat diets or low fat diets. Control mice were wildtype B6 mice. Glucose tolerance tests were performed at 5 week intervals after the start of diet, and body fat composition was monitored. Mice were sacrificed at 15 and 20 weeks. Serum was collected for analysis, and adipose tissue were harvested and analyzed for cellular components using flow cytometry.

**CONCLUSIONS**

There does not seem to be a clear expression of metabolic syndrome in our model of lupus mice. In fact, at 20 weeks, lupus mice had lower glucose measures. This is most likely due to their reduced adipose composition, which could either indicate wasting from the lupus disease or an impaired ability to store adipose. Perhaps what the lupus phenotype contributes to the metabolic syndrome is too subtle to see in our model.
GUNSHOT VICTIMS AT A MAJOR LEVEL 1 TRAUMA CENTER: A RETROSPECTIVE COHORT STUDY OF 566,499 EMERGENCY DEPARTMENT VISITS

ZACH YONEDA
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
Despite decades of research, gun violence remains a significant cause of mortality, morbidity and preventable healthcare spending. Disturbing trends in regards to the sex, age and race of gunshot victims have been established.

OBJECTIVES
1) Compare characteristics of gunshot victims in Nashville, Tennessee to the overall Emergency Department population and 2) Analyze association between gunshot wound and race.

MATERIALS AND METHODS
A retrospective cohort study of all Emergency Department visits from 2004-2009.

CONCLUSIONS
Our study reveals the majority of GSW in Nashville belong to young, male African-American victims of assault. These data support the need for policy directed intervention for specific groups.

MENTOR / DEPARTMENT
A. Alex Jahangir, MD, Vanderbilt University Medical Center-Department of Orthopedic Surgery and Rehabilitation Manish K. Sethi, MD, Vanderbilt University Medical Center-Department of Orthopedic Surgery and Rehabilitation

USE OF A NOVEL SMALL MOLECULE WNT INHIBITOR TO SLOW CANCER CELL GROWTH

LI ZHOU
LABORATORY-BASED BIOMEDICAL RESEARCH

BACKGROUND PROBLEM
The Wnt signaling pathway is evolutionarily conserved and plays a role in regulating key processes like cell morphology, motility, proliferation, and fate determination during embryonic development. In light of the Wnt pathway’s control over critical components in cell development and homeostasis, it is unsurprising to find that this pathway is mutated in 90% of colon cancers.

OBJECTIVES
The pathway’s widespread involvement in colon cancer makes it a potential target for novel drug therapy. We hypothesized that our novel Wnt inhibitor would selectively inhibit Wnt-dependent colon cancer cell lines.

MATERIALS AND METHODS
Various colon cancer cell lines, either with or without a Wnt-pathway mutation, were grown in 96 well plates. Different treatment groups received between 0 uM (DMSO control) to 20uM of our isolated Wnt-inhibitor. Cell titers were measured every 24 hrs over 72 hours using a luciferase based luminescence assay.

CONCLUSIONS
These results suggest that Windomorphin is a selective inhibitor of the Wnt pathway and may hold therapeutic potential in the treatment of Wnt pathway-mutated colon cancer cell lines.

ACKNOWLEDGEMENTS
Dr. Jijun Hao

MENTOR / DEPARTMENT
Dr. Charles Hong, Department of Cardiology
This educational experience is designed to introduce students to theory and practice in the learning and teaching of medical students, residents, practicing physicians and patients as well as provide an opportunity to develop a project in an area of interest.

Students will be provided with opportunities to examine the practice of education in a wide variety of health care settings. Students will have opportunities to examine:

- how learning occurs in medical school, residency, and practice
- how students can develop reflection and self-assessment skills to develop an approach to lifelong learning that can be used throughout their medical careers
- what teaching strategies help medical students, residents, practicing physicians, and patients learn
- assessing the progress of student, resident, or patient learning
- curriculum development in specific content areas

The student experience will introduce them to the community of scholars at Vanderbilt and elsewhere who study and work in the field of medical education. Each student will work with a mentor who will provide direction to the student as he or she determines an area of focus, develop a project proposal, implement the project proposal, present findings, and prepare findings for publication. In addition, students in the Medical Education area will be expected to participate in ongoing educational activities such as Medical Education Grand Rounds, Medical Education Journal Club, and CORE Conversations dealing with issues in medical education research.

"Working with students in the Emphasis Program has been one of the highlights of my work at Vanderbilt. It has been an honor and a privilege for me to share their excitement and satisfaction as they worked through and accomplished their projects. I look forward to working with the students who choose the Medical Education area this year."
FOCUS GROUP EVALUATION OF VANDERBILT PROGRAM IN INTERPROFESSIONAL LEARNING

KATIE COLLINS

MEDICAL EDUCATION

BRIEF DESCRIPTION
This project involves focus group evaluation of the new Vanderbilt Program in Interprofessional Learning, an educational model which places health professional students side by side in clinical settings from the beginning of their educational experience.

ACKNOWLEDGEMENTS
Josiah Macy Jr. Foundation for grant support of VPIL

MENTOR / DEPARTMENT
Bonnie Miller, M.D., Senior Associate Dean for Health Sciences Education, and Donald Moore, Ph.D., Director of Continuing Medical Education

AN EXAMINATION OF THE RIPPIT MOCK INTERVIEW PROGRAM AT VANDERBILT

LAURA TORTORA

MEDICAL EDUCATION

BRIEF DESCRIPTION
The interview is a key component of a fourth year medical student’s application to residency. However, medical students have limited experience in a formal interview setting. In 2009, Vanderbilt instituted the RIPPIT program in order to give fourth year medical students an opportunity to practice a typical residency interview and receive detailed feedback and advice from members of the VUSM faculty. The primary purpose of this study was to examine whether students who participated in the program felt that it was a worthwhile and useful experience.

MENTOR / DEPARTMENT
Michael Pilla, MD; Department of Anesthesiology

COMPASSION IN MEDICAL SCHOOL: AN AUTOETHNOGRAPHY

NATALIE NESMITH

MEDICAL EDUCATION

BRIEF DESCRIPTION
This project is a look into the development of compassion throughout medical school through the eyes of a student.

MENTOR / DEPARTMENT
Dr. Roy Elam, Center for Integrative Medicine Dr. Emil Petrusa, Medical Education
One area of inquiry in Bliton’s current research is directed toward the phenomenon other main campus programs interested in clinical ethics activities and experiences. Bliton also served as the Chief of VUMC's Clinical Ethics Consultation Service from 1994-2007. Within the Center for Biomedical Ethics and Society, he continues to work closely with students from Medicine, Philosophy, Religion, Divinity, as well as members of Vanderbilt University Medical Center's Ethics Committee since 1991. Bliton also served as the Chief of VUMC's Clinical Ethics Consultation Service from 1994-2007. Within the Center for Biomedical Ethics and Society, he continues to work closely with students from Medicine, Philosophy, Religion, Divinity, as well as other main campus programs interested in clinical ethics activities and experiences.

One area of inquiry in Bliton’s current research is directed toward the phenomenon of “self” and moral existence. The “self” is presupposed throughout our contemporary and classical references to the “person as person.” Similar concepts and languages about the “self” occur importantly in the background of talk about human bodies, about consciousness, politics, history, and medical science. Bliton’s research examines these areas because heated debates in bioethics—from abortion to discussions about the interface of genetics and neuroscience, informed consent and privacy, allocation of scarce resources, and so on—all make deep presumptions about the nature and social action of “self.”

Integral to his clinical focus, Bliton’s philosophical interests are wide ranging: from the exploration of ethical issues associated with innovative fetal therapies, such as the moral presence of a fetus and the maternal/fetal dyad, to the complexity of moral experience in the neonatal intensive care setting to considerations about making moral sense of withdrawing medical treatments. His work also considers the ongoing examination of the ethical basis for clinical interactions, premised on careful attention to the actual details and experiences associated with clinical relationships and decision-making.

It was not so much a specific question that was introduced to me by my first mentor, Jim Sheridan, rather than it was the way he was willing to approach questions. The lasting understanding gained from him was the deep and abiding commitment to a freedom of inquiry. Any question could be asked, especially if it was lively, real, and difficult. The range of inquiry as he used to say—whether in all seriousness or not—was “from angels to ash can.” If the question was difficult to ask because it might risk doing violence what was habitually thought of as accurate or correct, he would listen long before he might rephrase the question or suggest that I take even greater intellectual risk by asking it more vigorously and sharply. I mention this commitment because we live in a culture and at a time in which information is exchanged so rapidly and concerns for efficiency and conformity are so dominant that the idea of taking time to reflect on one’s own, our own, history and its questions, or to examine critically our own values, commitments, and beliefs—let alone the values, beliefs, and commitments of others—is not encouraged.

Yet, little else stands out as so crucial, especially to medicine, which not only operates with an implicit idea of what human being should be, but which contributes greatly to the images, both cultural and individual, about what is worthwhile to people. As Edmund Pelegino suggests, “medicine is at once the most humane of the sciences and the most scientific of the humanities.” The questions raised in that “at once” thus go to the very core of human understanding.

Mark J. Bliton, Ph.D., received his undergraduate degree in Philosophy and English from Allegheny College (BA, 1984) before studying Applied Philosophy at Bowling Green State University, OH (1985-1987) and then becoming a student of Richard W. Zaner at the Center for Clinical and Research Ethics. While working on his Ph.D. in the Department of Philosophy at Vanderbilt, Bliton also served as an Instructor of Medical Ethics in Vanderbilt’s School of Medicine. Bliton was co-founder (with Zaner) and then Chief of Service of the Clinical Ethics Program at Saint Thomas Hospital in Nashville (1991-1994). An Associate Professor in the Department of Medicine, with Secondary appointments to the Department of Philosophy and the Department of Obstetrics and Gynecology, Bliton has been a member of Vanderbilt University Medical Center’s Ethics Committee since 1991.

The medical humanities are not one discipline but many, including ethics, literature, history, religious studies and others. Each of these disciplines employs its own tools and methods. For example:

- **Bioethics/medical ethics** provides tools for analyzing and resolving quandaries in practice and policy, and for discerning the moral dimensions of medical practice.

- **History of medicine/science** provides tools and paradigms for placing contemporary medical practices and scientific knowledge into larger social-historical perspective.

- **Literature** provides models for understanding persons and events that draw upon affective and aesthetic domains of knowledge, for example, the variety of ways that narrative is used in medicine, and aids in understanding the experiences of both patients and physicians.

- **Religion/spirituality** provides strategies for appreciating the ways illness, suffering and death are interpreted by patients and their families and caregivers.

Medical humanities, ethics, and policy provide resources for both professional competence and also for personal and civic life. Historical perspective, literary imagination and ethical literacy can contribute substantially to good doctoring, but also to balance between professional and personal life, and to knowledgeable engagement in the larger community and society on health questions.
UNDERSTANDING OLD SECRETS: INSIGHTS INTO THE NEW WORLD OF THE PLACEBO EFFECT

STEFAN BUMOL
MEDICAL HUMANITIES, ETHICS & POLICY

OBJECTIVES
In recent decades the phenomenon traditionally referred to as the “placebo effect” has itself been the subject of rigorous scientific inquiry. The scientific community’s increasingly enhanced understanding of the neurobiological mechanisms of this phenomenon necessitates a comprehensive examination of its implications. This synthesis seeks to properly frame the placebo effect in its numerous anthropological and historical contexts in light of modern research into its mechanisms and ethics to ultimately reveal its important implications for the future of the therapeutic encounter and the healing relationship.

BRIEF DESCRIPTION
This paper provides a comprehensive review of the past, present, and future of humanity’s understanding of the placebo effect and synthesizes this information to reveal possible ways of utilizing new scientific knowledge to ethically enhance the efficacy of active treatment and trial design.

MENTOR / DEPARTMENT
Dr. Roy Elam, MD Director of the Vanderbilt Center for Integrative Health

MATTERS OF LIFE AND DEATH

CAROL DUH
MEDICAL HUMANITIES, ETHICS & POLICY

BRIEF DESCRIPTION
How the role of medicine in the death penalty debate reflects the role of medicine in broader ethical debate.

CONCLUSIONS
The issue whether an individual of reduced capacity can be culpable of his or her own actions has been thrust into the limelight in the wake of the recent Arizona shooting of Congresswoman Gabrielle Giffords. This conversation is of paramount importance, as the public discussion raises issues of mental illness in the context of a potential death sentence. Medicine continuously shapes law and society. As we make advancements in medical knowledge and understanding, the medical profession as a whole teaches society how to treat people better. A growing understanding of humans and humanity will always be the light that leads the way for evolving standards of decency that are society’s benchmark of progress.

MENTOR / DEPARTMENT
Christopher Slobogin, Vanderbilt Law School

HEALING AROUND THE FIRESIDE: A RETURN TO TRUE WHOLENESS AND COMPASSION THROUGH STORYTELLING

SUZANNE FOX
MEDICAL HUMANITIES, ETHICS & POLICY

OBJECTIVES
This project was an exploration of the problem of suffering and its opposite the experience of wholeness through the process of narration—experiencing, writing, editing, and retelling a story. The second aim was to study the role narrative medicine had in medical education both in the M1-M4 years and as part of continuing medical education efforts to prevent physician burnout and to foster more compassionate care.

BRIEF DESCRIPTION
Through exploring the process of narration—experiencing, writing, and retelling a story, physicians and health care workers restore their wholeness and thus have more to offer to each other and to each patient, this project explored narrative medicine as a process and how it might be implemented in a medical school curriculum.

MENTOR / DEPARTMENT
Roy Elam, MD Director Vanderbilt Center for Integrative Health & Larry Churchill PhD, Director of the Center for Biomedical Ethics and Society

HEALING SKILLS: THE UNDERSERVED PATIENT PERSPECTIVE

KATHLEEN NEMER
MEDICAL HUMANITIES, ETHICS & POLICY

OBJECTIVES
Studies have shown that in addition to the medicines or treatments given to patients, the relationship with the healthcare provider itself can be beneficial and therapeutic in helping patients get better. I propose to examine if patients receiving healthcare in a publically funded clinic, supporting a largely low income population, experience such a healing relationship with healthcare providers. I am particularly interested in what healthcare providers in an FQHC can do to demonstrate care, build trust and confidence, and help patients attain their ideal state of health. Specific Objectives: 1. To better understand how medically underserved patients experience and understand their relationships with their practitioners. 2. Identify barriers to the physician-patient relationship in a community health setting. 3. Identify positive factors of the physician-patient relationship that move toward healing.

BRIEF DESCRIPTION
Relationships between patients and practitioners are at the heart of healing and the quality of care, yet little is known about the factors that enhance or diminish these
relationships. The few studies that exist focus on general patient populations rather than on more vulnerable groups. The goal of this research was to identify physician actions and behaviors that facilitate good doctor-patient relations, from the perspective of the medically underserved patient. Twenty-five patients were interviewed at the United Neighborhood Health Services Northeast Clinic, one of seventeen Federally Qualified Health Centers in Nashville, TN serving an underinsured patient population. Patients were asked to tell the story of their relationship with their health care provider, and in so doing, to identify the qualities of engagement with their doctor that move beyond simple treatment of disease. Interviews were audio-recorded, professionally transcribed, made anonymous, and analyzed independently. Six physician actions emerged as vital to the doctor-patient relationship. As presented in the words of the patient, they are as follows: Sits down with me; Treats me like family; Makes me feel like I’m her only patient; Takes the time; Gets to the root of it; Will not turn me away. Patients desired a caring physician who not just helped them with their problems, but interacted with them on a human level. How the doctor made the patient feel was vitally important to the clinical encounter. It can be concluded that relationships between physician and patient are therapeutic in and of themselves, and that they serve a major role in healing and continuity of care, especially in the medically underserved patient population. Encouraging such interactional skills in practitioners will provide long-term improvements in patient care and reaffirm the medical profession as a healing art.

MENTOR / DEPARTMENT
Larry Churchill, PhD, Center for Biomedical Ethics & Society

BEST OUTCOMES: WHAT DOES IT MEAN TO FAMILIES?

BRITTANY M TAYLOR

MEDICAL HUMANITIES, ETHICS & POLICY

BRIEF DESCRIPTION
I spent the summer interning for Genetic Alliance exploring “best outcomes,” and what it means to families with special needs children.

CONCLUSIONS
Through this discussion, it was generally decided that best outcomes are, “a dynamic and flexible state that changes over time. It is an optimum state of health and well being that fosters the greatest potential and happiness for the individual.” Participants at the salon also agreed that anyone involved in the care of the child can determine the outcomes, but the outcome will vary based upon what lens one is looking through and based upon who the outcome is tailored to. Best practices and best outcomes are a continuum, but it is generally thought that one should first determine what the best outcome is and then design a best practice to achieve that specific outcome. Some other highlights of this summer experience were issuing policy recommendations for the organization, compiling best practice recommendations for Down syndrome, writing a narrative summary of scientific uses for residual dried blood spots, participating in the Genetic Alliance annual conference, and participating in a lobby day.

ACKNOWLEDGEMENTS
Genetic Alliance Sharon F. Terry, MA Alyson Krokosky, MS, CGC Dena Freeman, MPH

MENTOR / DEPARTMENT
Ellen Wright Clayton, MD, JD Rosalind E. Franklin Professor of Genetics and Health Policy Director, Center for Biomedical Ethics and Society

Natasha Bonhomme Genetic Alliance- Vice President of Strategic Development
Terence S. Dermody, M.D., is the Dorothy Overall Wells Professor of Pediatrics and Microbiology and Immunology, Director of the Division of Pediatric Infectious Diseases, Director of the Lamb Center for Pediatric Research, and Director of the Vanderbilt Medical Scientist Training Program (MSTP). Dr. Dermody came to Vanderbilt in 1990 after completing his medical degree at Columbia University in New York, a residency of internal medicine at Presbyterian Hospital in New York, and fellowships in infectious diseases and virology at Brigham and Women’s Hospital and Harvard Medical School in Boston. Dr. Dermody is a physician scientist with clinical interests in pediatric infectious diseases and research interests in viral pathogenesis. He has been directing the MSTP since 2003.

The central goal of the Medical Scientist Training Program (MSTP) at the Vanderbilt University School of Medicine is to train leaders in academic medicine. Our program is based on solid clinical and research training and is designed to foster the development of independent scientific careers.

The MSTP is a joint endeavor between the Vanderbilt University School of Medicine and the Vanderbilt University Graduate School. Students usually complete the first two years of Medical School, pursue graduate studies for three to four years, then return to Medical School to complete the final two years of clinical training. Successful completion of the program leads to both the M.D. and Ph.D. degrees.

Full-time laboratory research is performed in three rotations from the summer prior to the first medical year through the summer following the first year of Medical School. These cumulative research experiences serve as the Emphasis project for MSTP students.

“The laboratory rotations that comprise the Emphasis experience are incredibly important for our students. They gain exposure to a variety of research opportunities and select a mentor, training environment, and scientific project best suited to their professional development.”
BETA CELL PROLIFERATION AND REGENERATION IN ISLETS DOES NOT REQUIRE PANCREATIC SIGNALS OR MICROENVIRONMENT

KRISTIE AAMODT
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
In type 1 and type 2 diabetes, mellitus pancreatic islet beta cell mass is significantly reduced. Unfortunately beta cell regeneration is quite limited and new strategies are needed to promote this process. Using a bitransgenic mouse model of doxycycline-inducible VEGF overexpression in beta cells we have found that increased intra-islet endothelial proliferation is accompanied by beta cell loss and that doxycycline (Dox) withdrawal is followed by beta cell proliferation and islet regeneration.

OBJECTIVES
To determine if this islet regeneration is dependent on pancreatic signals or the microenvironment. We tested whether islet regeneration could occur in islets transplanted at an extra-pancreatic site.

MATERIALS AND METHODS
Bitransgenic and wild-type islets were transplanted beneath the kidney capsule of bitransgenic mice. After a two week engraftment period endogenous pancreas and transplant grafts were collected after 1 week Dox treatment, two, and three weeks after Dox withdrawal. Immunofluorescent staining of the samples for insulin, Ki67, VEGF, CD31, and DAPI was performed and analyzed for VEGF induction, islet morphology, and beta cell proliferation.

RESULTS
Just as it did in bitransgenic islets of the endogenous pancreas, Dox induced VEGF expression, endothelial cell overgrowth, and beta cell loss in transplanted bitransgenic islets. Upon Dox withdrawal, islet morphology and vasculature normalized, and the percentage of proliferating beta cells was greater in bitransgenic grafts compared to wild-type grafts. None of these effects were observed in wild-type islets transplanted into the contralateral kidney.

CONCLUSIONS
Beta cell proliferation and islet regeneration in transplanted islets was similar to that in islets within the pancreas indicating that the stimulus for beta cell proliferation is not dependent on the pancreatic environment. In addition, the stimulus is not due to a circulating humoral factor since no beta cell proliferation occurred in wild-type islets. Instead, it must be dependent on the local microenvironment with increased endothelial cells and/or cells recruited to the VEGF-overexpressing islet. Understanding the signals that promote islet regeneration in diabetes is dependent on pancreatic signals or the microenvironment. We tested whether islet regeneration could occur in islets transplanted at an extra-pancreatic site.

ACKNOWLEDGEMENTS
Marcela Brissova, Ph.D., Alvin Powers, M.D., Greg Poffenberger, Anastasia Golovin, Alena Shostak, and the Vanderbilt MSTP

MENTOR / DEPARTMENT
Alvin C. Powers, M.D., Department of Molecular Physiology and Biophysics

EVIDENCE-BASED KNOWLEDGE MAINTENANCE FOR DIAGNOSTIC DECISION SUPPORT
RAVI ATREYA
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
The amount of medical knowledge is growing at an exponential rate. Because physicians commonly experience clinical knowledge and data overload, it is not surprising that studies have shown that their clinical knowledge declines over time post-training. Computers are necessary to manage and present data in useful ways to physicians in practice and training. Decision support systems are only as good as the base of medical knowledge that supports it. A knowledge-base is an organized medical information warehouse that includes medical terminology, such as various findings, diseases, and diagnostic procedures, and the relationships between those terms. Manual knowledge base development has consumed up to 20 person-years of work for individual experienced physicians. The difficult construction process makes it cumbersome to manually update such knowledge-bases. Partial or complete automation of knowledge-base construction will be vital to the long-term viability of decision and education support systems.

OBJECTIVES
My goal is to develop new approaches to building and maintaining clinical knowledge-bases. The specific result for this work will be a system that helps human experts to maintain a knowledge-base that serves as the basis for a general, internal-medicine diagnostic decision support system.

MATERIALS AND METHODS
The knowledge base derivation algorithms will involve semi-automated guided review of relevant literature and of de-identified medical records at Vanderbilt University Medical Center. Data will be extracted from these sources using natural language processing algorithms. The results will be used to provide expert clinician reviewers with tools to facilitate knowledge-base construction.

RESULTS
To be determined over the next 3 to 4 years.
CONCLUSIONS
This research will help to create and maintain an information resource. It will have an impact in enhancing medical education and increasing the efficiency and quality of medical practice through diagnostic decision support.

ACKNOWLEDGEMENTS
Randolph A. Miller, M.D. and the Vanderbilt MSTP

MENTOR / DEPARTMENT
Randolph A. Miller, M.D., Department of Biomedical Informatics

ESTIMATION OF TYPE I ERROR IN AN AMISH PEDIGREE GENETIC ANALYSIS

LAURA D’AOUST
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
Alzheimer Disease (AD) is the most common neurodegenerative disease in the USA. In order to further understanding of the disease and develop targeted therapies, focus has been place on elucidating the genetic factors that increase risk of disease development. Studying a genetically isolated founder population, like the Amish communities of Ohio and Indiana has many advantages for elucidating AD risk genes. Due to the complex pedigree structure, the statistical analysis is complicated. To evaluate statistical methods, simulation studies can be useful to estimate parameters such as false positives or type I error rates.

OBJECTIVES
The aim of this study was to estimate the type I error rate of association analyses in a complex Amish pedigree structure.

MATERIALS AND METHODS
GenomeSIMLA-Amish is a simulation package for generating SNP data and hospital costs. It is estimated that inpatient testing represents a quarter of total hospital costs. As a result, it is important to examine medical practice in order to provide better care and maximize efficiency in the hospital. De-identified patient data at Vanderbilt can provide insight into drug prescription and lab ordering habits. Both sets of data can be correlated with the patient’s disease in order to explore patterns in the data. The knowledge base and the patterns that are derived from it can be used to develop decision support tools in the future to provide better care and increase the efficiency of resource utilization in the hospital.

OBJECTIVES
The goal of this project was to develop a knowledge base that relates drugs and labs to disease. Patterns that are extracted from this can be used to identify areas of clinical practice or hospital management that can be targeted by adding to the CPOE (care provider order entry) system.

MATERIALS AND METHODS
De-identified patient data at Vanderbilt from Aug 1999 to July 2003 inclusive has been collected and loaded into a secure database. The lab order and drug prescription data was collected for each patient. This data was correlated with the ICD9 codes for each patient to create a set of drugs/labs and diseases. The drug and ICD9 code data were categorized in order to create larger sample sets. The prescription/order data for each disease was normalized against the rate of prescription/order of all diseases.

RESULTS
There are 1819887 lab orders and 147879 prescriptions in the database. This data is spread over 61179 patients. There are 15421 combinations of drug (with drug count) and ICD9 categories. There are 9010 combinations of lab (with lab order count) and
ICD9 categories. There are 152 ICD9 categories derived from the standard splits of codes. The data was normalized, resulting in ratio’s of the rate the drug/lab was ordered for the disease category against the rate the drug/lab was ordered over the entire patient population.

CONCLUSIONS
Drugs and lab orders have been correlated with disease categories, and while there is still noise in the results, there are steps that can be taken to fix this problem. The data was initially normalized due to the fact that there were a set of drugs that were ordered for most patients in the hospital regardless of the disease. This included H2-blockers, opiates, and anti-anxiety medication. After the normalization process, the drugs and labs are far more disease specific. However there is still some noise relating to incidence of a disease as well as the rate at which certain drugs are ordered and re-ordered. Future work will be conducted to set a variety of thresholds to remove the noise from the data.

MENTOR / DEPARTMENT
Randolph A. Miller, Ph.D., Department of Biomedical Informatics

INTRAISLET CELLULAR INTERACTIONS WITHIN PANCREATIC ISLETS OF LANGERHANS: THE INFLUENCE OF β-CELLS ON α-CELL FUNCTION

TROY HUTCHENS
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
Pancreatic islets are endocrine micro-organs that regulate serum glucose levels through the secretion of systemic hormones, most notably insulin and glucagon. Insulin is secreted by β-cells at high glucose levels and acts on muscle, liver, and adipose tissue, causing them to take up serum glucose. Glucagon is secreted by α-cells at low glucose levels and acts on the liver, which converts glycogen into glucose, which is released into the serum. Euglycemia is maintained through a dynamic balance of insulin and glucagon secretion, which fluctuate in response to serum glucose levels, hormonal, and neuronal stimuli. Diabetes is caused by pancreatic islet dysfunction, and is a major and escalating cause of morbidity and mortality both in the US and worldwide. Diabetes has traditionally been thought of as β-cell/insulin problem and has been treated as such. Recently however, α-cell dysfunction, observable as deregulated and excessive glucagon secretion, has shown to contribute to hyperglycemia in diabetic patients. In isolated α-cells and in advanced diabetes, glucagon secretion is no longer inhibited by high glucose concentrations. This indicates that intraislet cellular interactions may be necessary for normal α-cell function.

OBJECTIVES
This research will further elucidate the interdependent molecular physiology of pancreatic islets by studying the interactions between the various cell types within islets. Specifically, this research will address the understudied influence of β-cells on α-cell function.

MATERIALS AND METHODS
Advanced microscopy techniques allow for the detailed study of mouse pancreatic islet physiology, not limited to redox state as a marker of metabolism, intracellular calcium levels, and cell type identification and sorting through the expression of fluorescent proteins.

RESULTS
To be determined.

CONCLUSIONS
To be determined.

ACKNOWLEDGEMENTS
Sylvan Le Marchand, Ph.D., and David W. Piston, Ph.D.

MENTOR / DEPARTMENT
David W. Piston, Ph.D., Department of Molecular Physiology and Biophysics

GENE-GENE INTERACTIONS ARE ASSOCIATED WITH BASELINE MRI MEASURES IN ALZHEIMER’S DISEASE NEUROIMAGING INITIATIVE (ADNI)

MARY ELLEN KORAN
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
Genetic studies often use binary disease status (present/absent) as the primary phenotype, or outcome variable. However, studies of complex disease require rich phenotypic information that can be mapped to distinct genetic etiologies, which may involve gene-gene or gene-environment interactions. For brain-based diseases, such as Alzheimer disease, neuroimaging can provide such phenotypic measures, many of which have been shown to correlate with disease status and to have greater sensitivity in detecting early pathological changes.

OBJECTIVES
In this study, we aimed to test for the association of gene-gene interactions with MRI measures related to Alzheimers disease using data from the Alzheimer’s Disease Neuroimaging Initiative (ADNI).

MATERIALS AND METHODS
The ADNI dataset includes information on rates of change in cognition, function, brain structure and biomarkers in 200 elderly controls, 400 subjects with mild cognitive impairment, and 200 patients with mild AD. We used linear regression analysis to test the ability of 45 previously-implicated SNP-SNP interaction models to predict 38 different brain region volume and thickness measurements related to AD.

RESULTS
We were able to replicate 6 out of
the 45 models in at least 26 of the 38 regions brain regions. These included NMDA receptors GRIN2A and GRIN2B, protein tyrosine phosphate receptors PTPRN2 and PTPRD, sortilin-related receptors SORCS1 and SORCS2, and ERBB4 and INSR

CONCLUSIONS
Ultimately using imaging genetics, we hope to identify both genetic and brain-based markers that indicate a predisposition to AD. AD is diagnosed late in disease progression, and current pharmacological therapies are useful only in early stages of disease. If such markers could identify high-risk individuals who should start treatment earlier, progression of this devastating disease could be slowed, with substantial benefit to patients and their families, as well as cost-savings to society.

ACKNOWLEDGEMENTS
Vanderbilt MSTP

MENTOR / DEPARTMENT
Tricia A. Thornton-Wells, Ph.D., Center for Human Genetics Research

INDUCED PLURIPOTENT STEM CELL STUDY OF GENE-ENVIRONMENT INTERACTIONS IN PARKINSON’S DISEASE
KEVIN K. KUMAR
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
The long-term goal of this research is to enable personalized toxicological profiling to provide patient-specific risk assessment for environmental neurotoxicants. Human Induced Pluripotent Stem Cells (hiPSCs) are highly similar to embryonic stem cells and can be differentiated in culture into multiple cell types including neurons. These hiPSCs and neurons derived from them may reflect the unique genetic blueprint of the individuals from which they are generated. Thus this technology opens the opportunity, for the first time, to characterize the physiological, toxicological, pharmacological and molecular properties of living human neurons with identical genetic determinants as human patients.

OBJECTIVES
Parkinson’s Disease (PD) is a progressive neurological disorder caused by the degeneration of the dopaminergic neurons in the substantia nigra pars compacta and the ensuing loss of striatal dopamine innervation. This study seeks to investigate changes in cellular metabolism and effects of toxicants in neurons differentiated from iPSCs derived from PD patients.

MATERIALS AND METHODS
Biopsies of patients with PD and controls were performed to obtain primary human dermal cells, the source material for patient-derived hiPSCs. In addition, several lines were derived from patients lacking a functional PARK2 allele (associated with early onset and juvenile PD). Lentiviral vectors were then used to transduce fibroblasts into hiPSCs. hiPSC lines were validated through analysis of pluripotency marker expression and karyotyping. Subsequently, hiPSCs were used to generate neural progenitors and differentiated neurons for these studies.

RESULTS
We have currently demonstrated that neuroprogenitors derived from PARK2 mutant hiPSC lines were more sensitive to Cu2+ than control cells. Furthermore, cytotoxicity of three other neurotoxic metals was not significantly different between these lines. This finding demonstrates that neurotoxicological analysis in hiPSC-derived human neuronal cells can reveal genotype-phenotype differences. Our current goal is the differentiation of hiPSCs into mid-brain dopaminergic neurons for further analysis of their response to environmental toxicants.

CONCLUSIONS
In summary, this project hopes to reveal the toxicant profile of neurons differentiated from iPSCs derived from PD patients. These results have significant clinical implications, including the identification of novel therapeutic targets, the development of stem cell transplants, and the construction of screening profiles to determine PD prognosis.

MENTOR / DEPARTMENT
Aaron Bowman, Ph.D., Program in Neurosciences

WO PHAGE ENDOLYSIN AS AN ANTIBACTERIAL FOR WOLBACHIA
JASON METCALF
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND PROBLEM
Wolbachia is a Gram-negative, obligate intracellular genus of bacteria that is one of the most widespread infections known. Wolbachia is a reproductive parasite in arthropods, but is required for reproduction and larval development in filarial nematodes that cause lymphatic filariasis and river blindness. WO is a bacteriophage that infects Wolbachia, either as a prophage, or occasionally as a lytic phage capable of killing Wolbachia. The phage gene responsible for lysing Wolbachia is an endolysin that digests the cell wall in order to lyse the cell and release phage progeny. Endolysins typically require a second protein, a holin, in order to gain access to the cell wall through the inner cell membrane, but some do not.

OBJECTIVES
Express and purify endolysin from the phage species wRi1 WO and evaluate its effectiveness at killing Wolbachia in culture.

MATERIALS AND METHODS
A tagged wRi1 WO endolysin
gene was previously cloned by Lisa Funkhouser. The gene was transformed into E. coli and expressed. Endolysin protein was then purified with a nickel column and added to in vitro cultivated Wolbachia at varying concentrations. Bacterial lysis was evaluated with a Live/Dead viability stain. E. coli in culture was used to test the specificity of the lysin among other gram-negative infections.

RESULTS
Purified endolysin lysed Wolbachia cells at a concentration of 400 ug/mL, while it was unable to lyse E. coli unless added at a higher concentration of at least 4 mg/mL.

CONCLUSIONS
wr1 WO endolysin may be useful as a semi-selective antibacterial against Wolbachia and filariid-associated diseases. The endolysin probably contains a signaling sequence or other functional domain that allows it to access the cell wall without a holin. Further studies will evaluate if the endolysin can kill Wolbachia inside its host, the specificity of the lysin, and why it functions without a holin.

ACKNOWLEDGEMENTS
Bordenstein lab, especially Lisa Funkhouser and Kristin Jemigan; Vanderbilt MSTP

MENTOR / DEPARTMENT
Seth Bordenstein, Ph.D., Department of Biological Sciences

OBJECTIVES
Characterizing EML4-ALK variants in non-small cell lung cancer

CAROLINE NEBHAN
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
In recent years, molecular targets have been identified in cancers that enable the use of more specific targeted therapies. Lung cancers are now commonly screened for known, treatable oncogenic driver mutations, such as EGFR mutations. Activating fusions involving the gene encoding the ALK tyrosine kinase were discovered in lung cancers in 2007. An ALK tyrosine kinase inhibitor in clinical development has already shown highly promising activity against lung tumors harboring ALK fusions.

OBJECTIVES
The echinoderm microtubule-associated protein-like 4 gene (EML4) is most commonly fused to ALK in lung cancers. Currently, at least nine different fusion variants of EML4-ALK have been identified. In all variants, fusion occurs at exon 20 of the ALK gene, and the kinase domain is preserved. However, the variants contain different truncated forms of the EML4 gene. In this study, we sought to examine the protein products of three EML4-ALK fusion variants to determine any differences in their biologic activity. Whether the variable portion of EML4 matters is currently unknown.

MATERIALS AND METHODS
cDNA expression constructs encoding flag-tagged EML4-ALK fusion variants, V1 (E13;A20), V2 (E20;A20) and V3b (E6b;A20) were transiently transfected into HEK293 cells using Lipofectamine. Lysates from HEK293 transfecants were examined by immunoblotting for total ALK protein expression, phosphorylated tyrosine (pTyr) and ALK-Y1604 residues, and flag levels.

RESULTS
All the cDNAs encoding various ALK fusions expressed appropriately-sized flag-tagged proteins. As a surrogate gauge of kinase activity, we measured the levels of "autophosphorylated" Y1604 on ALK by using a phospho-specific antibody. The expressed proteins appeared active, as indicated by the presence of phosphoALK in transfected cells and multiple induced tyrosine-phosphorylated proteins compared to lysates from cells transfected with vector controls.

CONCLUSIONS
The immunoblots performed thus far indicate that our cDNA expression constructs express appropriately sized and activated ALK fusion proteins when transfected into HEK293 cells. In future studies, we plan to determine whether these different variants display any biological differences that may be clinically relevant.

ACKNOWLEDGEMENTS
William Pao, M.D., Ph.D. and Christine Lovly, M.D., Ph.D.

MENTOR / DEPARTMENT
William Pao, M.D., Ph.D., Department of Cancer Biology

OBJECTIVES
BVES is underexpressed in colorectal carcinomas and reexpression promotes epithelial phenotype

BOBAK PARANG
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
It is well-established that adherens junctions are required for suppressing epithelial-mesenchymal transition (EMT) and metastatic progression in carcinoma, but the role of tight junctions (TJ) remains unclear in promoting EMT and metastasis. BVES, a TJ associated protein, is significantly underexpressed in all stages of colorectal carcinoma (CRC). In addition, BVES reexpression in CRC cells lines promotes an epithelial phenotype. The focus of this project is to elucidate the role of BVES in carcinogenesis.

OBJECTIVES
In order to understand the role of BVES in colorectal carcinogenesis, the ability of BVES to modulate WNT signaling and inflammatory carcinogenesis must be investigated. Potential interacting proteins must also be identified in order to better
characterize the role of BVES.

MATERIALS AND METHODS
1. Test the ability of BVES to modulate WNT signaling by interbreeding BVES-/- mice with APCmin mice and assessing for the impact on tumor burden. 2. Test for the ability of BVES to modulate inflammatory carcinogenesis by applying the AOM/DSS intestinal inflammatory carcinogenesis protocol to the BVES-/- mice. 3. A yeast two hybrid screen to identify potential BVES interacting proteins.

CONCLUSIONS
To be determined.

CONCLUSIONS
In summary, the goal of our project is to investigate the role of BVES in colorectal carcinogenesis by characterizing its interactions with the Wnt pathway, and by measuring its ability to modulate inflammatory carcinogenesis.

ACKNOWLEDGEMENTS
Vanderbilt MSTP
MENTOR / DEPARTMENT
Christopher Williams, M.D., Ph.D., Department of Cancer Biology

UNDERSTANDING THE FUNCTION OF MOTOR NEURON-DERIVED SONIC HEDGEHOG IN THE DEVELOPING EMBRYO

KAITLYN RYAN
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
The secreted morphogen Sonic Hedgehog (Shh) is critically important for proper organ formation and patterning in the developing embryo. Floorplate-derived Shh is known to specify the position and identity of neuronal precursors in the developing spinal cord. Located in the ventral neural tube, motor neurons require high levels of Shh in order to develop properly. Interestingly, once formed, motor neurons themselves express Shh, albeit at far lower levels than floorplate cells. Nonetheless, the function of motor neuron-derived Shh is not yet known, and identifying the potential cell populations targeted by motor neuron-derived Shh may ultimately lead to an improved understanding of both motor system development and motor disease pathogenesis.

OBJECTIVES
To determine the function and target cell population(s) of motor neuron-derived Sonic Hedgehog in the developing embryo.

MATERIALS AND METHODS
In situ hybridization for Shh mRNA was performed on wild type embryos at multiple stages of embryonic development. Shhcre; ROSA-YFPmembrane mice, in which Shh-expressing cells are YFP-labeled, were analyzed to verify Shh-expression in motor neurons. Potential tissue populations targeted by motor neuron-derived Shh were identified using mouse strains in which beta-galactosidase expression is driven by the Gli1 and Ptch1 promoters, two genes known to be expressed in Shh-responding cells. Finally, a mouse strain harboring a motor neuron-specific deletion of Shh (Olig2-cre; Shhflox/-) was generated and characterized for developmental defects.

RESULTS
Immunohistochemical studies of Shhcre; ROSA-YFPmembrane animals confirmed Shh expression in motor neurons innervating the fore- and hindlimbs at embryonic days 11.5 and 12.5. Although Shh protein could not be detected in motor neuron cell bodies, it appeared to be enriched in limb mesoderm proximal to motor neuron axon termini in E12.5 animals. Gli1lacZ and Ptch1lacZ analysis are ongoing. Olig2-cre; Shhflox/- animals appear to be viable, although more extensive characterization is ongoing.

CONCLUSIONS
The distribution of Shh protein in limb mesoderm suggests that Shh may be delivered, via motor neuron axons, to developing hypaxial musculature. However, additional studies are needed to confirm the effects of Shh on muscle development.

ACKNOWLEDGEMENTS
The Chiang Lab and the Vanderbilt MSTP.

MENTOR / DEPARTMENT
Chin Chiang, Ph.D., Department of Cell and Developmental Biology

ELUCIDATION OF GPCR STRUCTURE AND ANALYSIS OF SNP EFFECTS USING PROTEIN SECTOR DETERMINATION

PEDRO TEIXEIRA
MEDICAL SCIENTIST TRAINING PROGRAM

BACKGROUND
Protein structure is classically divided into four groups from primary to quaternary. These classifications only take into account the static 3-dimensional structure of a protein. However, it is possible with mathematical analysis of multiple sequence alignments to detect correlations between amino acid sites and compile those into discrete and nearly independent networks. These networks - “protein sectors” are comprised of contiguous amino acids in a protein’s 3-dimensional structure. We believe it is possible to apply this knowledge of evolutionary entanglement between sites to predict structure and assist in the evaluation of a SNP’s importance to protein function.

OBJECTIVES
My first aim is to implement within
the BioChemistry Library (BCL) a function to predict amino acid contacts within a protein, based on the identification of proteins sectors using multiple sequence alignments. I would then use these contact predictions as additional constraints on G-protein coupled receptors (GPCR) structure predictions. GPCRs are the targets of a majority of pharmaceuticals but because they are membrane proteins it is very difficult to determine such structures using traditional methods. My second aim is to analyze the networks identified using both the contact maps implied by the protein sectors as well as structural predictions for the GPCRs. These network determinations can then be shared with the scientific community via a database and webserver. My third aim is to collaborate to apply these internal GPCR networks to the study of SNP significance. An analysis of the SNP’s location and amino acid alteration in relation to the protein sector should be related to the magnitude of the effect.

MATERIALS AND METHODS
The Meiler lab has an extensive biochemical library of functions written in C++ to analyze data for protein structure prediction, multiple sequence alignments (bcl::align), and many other relevant tools. In addition, I’ll be using principle component analysis and other mathematical filtering techniques to de-noise the evolutionary data.

RESULTS
To be determined.

CONCLUSIONS
To be determined.

REFERENCES

ACKNOWLEDGEMENTS
Jens Meiler, Ph.D. and the Vanderbilt

MATERIALS AND METHODS
Three monoclonal antibodies (NKp46, CD49, and NK1.1) were tested using flow cytometry at different concentrations to determine the most effective antibody concentration to detect NK cells. After depleting NK cells with monoclonal antibody, viral titer will be measured by infectious focus assay or quantitative PCR (control animals will be administered isotype control antibody). Lung histopathology and weight loss post-infection will be used as measures of disease severity. Finally, the role of NK cells in innate immune responses will be determined by measuring cytokine expression using RT PCR.

REMARKS
NKp46 was determined to be the most efficient monoclonal antibody for detecting NK cells. NK cells were successfully depleted by administering three doses (200ug/dose) of NK1.1 antibody. The effects of NK cells on the innate and adaptive immune responses have yet to be determined.

FUTURE DIRECTIONS
In summary, the goal of this project is to determine the role of NK cells in innate and adaptive responses to HMPV infection. Possible future directions include measuring neutralizing antibodies, CD8+ T cells specific for NK cells, and studying the relative degrees of T helper Type I and Type II responses.

MENTOR / DEPARTMENT
John V. Williams, M.D., Department of Microbiology and Immunology

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The area of Patient-Oriented Research addresses:
1. The mechanisms of human disease,
2. Therapeutic interventions,
3. Clinical trials,
4. The use of new technologies for the diagnosis, treatment, or prevention of disease, and
5. The emotional, social, development and behavioral mechanisms of health and disease.

In addition to standard randomized clinical trials, patient-oriented methodologies also include self-perception measures (e.g., patients completing questionnaires), interviews, and focus groups. The core of this focus group is the scientific study of human participants to understand the cause of disease, health, and function. This understanding contributes to therapy and prevention. Clinically derived scientific knowledge, laboratory science, and patient-oriented science are core disciplines of the medical profession.

“The Emphasis Program provides me a unique opportunity to nurture aspiring medical students in the field of clinical research. The motivation to learn from each clinical encounter, fostered by the patient-oriented research of the Emphasis Program, is likely to transform each participating student into a life-long learner, effective problem-solver, and compassionate thinker. To paraphrase William Osler, ‘No matter trifling the clinical question at hand, answer it with a feeling that is demands the best that it is in you, and when done look it over with a critical eye, not sparing a strict judgment of yourself.’ Through the auspices of the Emphasis Program, I wish to inculcate such a spirit of reflection in each medical student.”

“**The Emphasis Program provides a unique opportunity to nurture aspiring medical students in the field of clinical research.**”
A LONGITUDINAL STUDY OF CA-MRSA NASAL COLONIZATION IN COLLEGE SPORTS PARTICIPANTS

ANDY ALENTZER

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM

Staphylococcus aureus (SA), a ubiquitous microorganism occupying the nares of nearly one-third of the human population, is the leading cause of skin, soft-tissue, and bone infections and has a spectrum of illness ranging from boils and cellulitis to disseminated disease and death. The problem of SA has been compounded in recent years by the development of community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA), providing the organism with a range of virulence factors and resistance to commonly used anti-staphylococcal antimicrobials. The frequency of CA-MRSA infections is increasing in children, adolescents, and sports team participants. Staphylococcal colonization increases the frequency of Staphylococcal disease, particularly for CA-MRSA, and in certain high-risk populations. Disease-causing isolates of CA-MRSA may possess a unique repertoire of virulence factors compared with carriage isolates.

OBJECTIVES

To determine the frequency of nasal and extranasal carriage of S. aureus and CA-MRSA in a cohort of healthy sports team participants during the course of two seasons; to determine the frequency of staphylococcal infections in carriers of CA-MRSA and carriers of methicillin-susceptible S. Aureus (MSSA), and to identify virulence factors associated with CA-MRSA colonization and infection.

MATERIALS AND METHODS

Nasal and oropharyngeal cultures for staph were obtained in 340 student athletes and 12 athletic trainers every month for a two-year period of time. Isolates confirmed to be MRSA underwent testing for presence of mecA gene and subsequent SCCmec typing. Genomic DNA was used as a template for polymerase chain reaction detection of the nuclease gene (specific to S. aureus) and the staphylococcal-specific cytotoxin Panton-Valentine leukocidin (PVL) using previously validated primers. Repetitive-element, sequence-based polymerase chain reaction (Diversilab System; Biomerieux, Durham, North Carolina) was used to determine genetic relatedness between strains and classification of genotype (eg, USA100, USA300).

CONCLUSIONS

MRSA colonization was extremely common in this cohort of collegiate athletes. MRSA infections were infrequent, though they corresponded to periods where MRSA colonization, particularly colonization with the epidemic USA300 CA-MRSA clone, was increased. This suggests that non-USA300 MRSA carriage is not a significant risk factor for staphylococcal SSTI in student athletes and that prevention strategies should focus on the relative presence of USA300 CA-MRSA strains in high-risk groups.

ACKNOWLEDGEMENTS

Elizabeth Saye

MENTOR / DEPARTMENT
Dr. Buddy Creech, Pediatric Infectious Disease

THE EFFECT OF PRIMARY CARE INTERVENTIONS ON CHILDREN’S MEDIA VIEWING HABITS AND EXPOSURE TO VIOLENCE

JILL ARAGON

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM

The American Academy of Pediatrics recommends that parents limit media viewing and children’s exposure to violence.

OBJECTIVES

To determine if brief primary care interventions can affect children’s media viewing habits and exposure to violence.

MATERIALS AND METHODS

English and Spanish speaking caregivers of 2 to 12 year old children presenting to a pediatric primary care clinic for a well-child visit were randomized to a 5 minute video intervention, hand-out intervention, or control at triage (1:1:1 ratio). Caregivers randomized to the 5 minute video intervention (n=107) were instructed to watch Decrease Exposure to Violence from the Play Nicely program. Caregivers randomized to hand-out intervention (n=114) were instructed to read the AAP recommended hand-out Pulling the Plug on TV Violence. Spanish versions of both of these interventions were provided to Spanish speaking caregivers. Caregivers in the control group (n=114) received standard of care. After their clinic visit, caregivers were asked to participate in a research study that included a follow up telephone survey in 2 weeks; 335/336 agreed.

CONCLUSIONS

Brief primary care interventions can affect children’s media viewing habits. These results have implications for how to improve primary care offerings related to children’s media exposure and violence prevention.

ACKNOWLEDGEMENTS

Molly White

MENTOR / DEPARTMENT
Seth Scholer
A NOVEL ASSESSMENT METHOD FOR CLASSIFYING ACROMIOCLAVICULAR SEPARATIONS: INTER- AND INTRA-RATER RELIABILITY AND REPRODUCIBILITY

TYLER ARMSTRONG

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Acromioclavicular (AC) separations are commonly classified using the Rockwood modified method, grading injury severity from 1 through 6. However, it is unknown whether this method is reproducible or reliable amongst clinicians.

OBJECTIVES
The purpose of the current study is to determine the accuracy of this classic evaluation method, and to propose an alternative method of injury evaluation using specific radiographic measurements.

MATERIALS AND METHODS
We evaluated the radiographs of 21 subjects (21 injured shoulders, and 21 control shoulders, 42 total) in a blinded fashion. A panel of 3 raters classified the injury severity as 1, 2, 3, or 5, and evaluated the standardized radiographs using a digital caliper to determine an AC injury severity ratio (coracoclavicular gap width / clavicular width). The AC injury ratio was correlated to the standard classification method, to determine average measurement ranges. The reliability and reproducibility of the two methods were then evaluated using standard statistical methods.

CONCLUSIONS
Existing methods of AC injury severity classification have moderate accuracy amongst clinicians. A novel method is proposed that may be more accurate and reproducible, and may have utility not only in initial injury evaluation, but also in reporting results of treatment.

MENTOR / DEPARTMENT
Minnesota Orthopedic Sports Medicine Institute, Edina, MN: Gregory N. Lervick, MD, Russell Giveans, PhD, Joseph McCormick, MD, Charles Popkin, MD.

EFFORTS TO IDENTIFY GENETIC CAUSE OF A CONGENITAL HEART DISEASE CASE: A BEDSIDE TO BENCH STORY

NATALIE AUSBORN

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
In the majority of congenital heart disease cases, etiology is unknown. Sporadic and heritable genetic causes are suspected, with likely contributions from environmental factors. Hypoplastic left heart syndrome (HLHS), which accounts for 8% of all congenital heart disease, has been associated with several genes (GJA1, NKX2.5, NOTCH1, and HAND1). A less common congenital heart disease, heterotaxy, has also been linked to GJA1 mutations. GJA1 encodes for connexin43, a gap junction protein with crucial role in contraction of heart and embryonic development.

OBJECTIVES
The previous associations between GJA1 and HLHS and heterotaxy are controversial; however, identification of a set of twins at Vanderbilt with either syndrome suggests a common genetic etiology. We thus hypothesized that a mutation in the GJA1 gene could explain both HLHS and heterotaxy in these twins and aimed to use a traditional candidate gene sequencing approach to identify possible mutations in GJA1.

MATERIALS AND METHODS
DNA was extracted from whole blood collected from Twin A with HLHS. Polymerase chain reaction was used to amplify GJA1 exons, where Exon 1 is a 300 base pair segment in the 5’ untranslated region and Exon 2 is a 2.8 kilobase region containing the codon. Amplified exons were sequenced by GenHunter and then aligned with a reference sequence from the National Center for Biotechnology Information with the online program ClustalW.

CONCLUSIONS
A mutation in Exon 1 or Exon 2 of GJA1 gene is not a possible etiology for HLHS in Twin A. Our next step will be to use Next Generation sequencing, a revolutionary platform for massive sequencing that generates short (75-100 base pairs) reads from tens of millions of DNA fragments, to sequence the whole exome of these twins and their parents to look for other possible causative mutations. In cases where traditional testing is not enough, Next Generation sequencing of the whole exome can link specific inherited heart diseases with previously unknown gene variations.

ACKNOWLEDGEMENTS
I thank Yan Ru Su, M.D., Cardiology Core Lab Director, for her instruction and guidance and David P. Bichell, M.D., for providing the clinical case. I would also like to thank Jared LeBoeuf, M.S., Cardiology Core Lab Manager, for his assistance with lab techniques and Jean Pfotenhauer, M.S., Genetic Counselor, for her assistance with collection of family history and pedigree drawing. This project was supported by NIH T35 Summer Research Training Program in Heart, Lung, and Vascular Biology. I appreciate Larry Swift, Ph.D., and Marnie McNamara’s assistance with this program.

MENTOR / DEPARTMENT
Charles Hong, M.D., Ph.D., Department of Cardiovascular Medicine

ANATOMIC AND VISUAL OUTCOMES FOLLOWING VITRECTOMY FOR VITREOMACULAR INTERFACE DISORDERS

SANDEEP BHAVE

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
The vitreomacular interface, made of the posterior cortical vitreous and the internal limiting membrane (ILM) of the retina, plays a critical role in the pathoetiology of multiple vision-threatening retinal disorders. Complete removal of the posterior cortical vitreous is essential for optimal surgical success.
OBJECTIVES
To investigate the anatomic and visual outcomes following vitrectomy and epiretinal membrane (ERM) removal (if indicated) for vitreomacular interface disorders (VID), with and without removal of the (ILM).

MATERIALS AND METHODS
We reviewed consecutive records of patients undergoing vitrectomy for VID. The primary outcome measures were change in best-corrected visual acuity at 6 and 12 months postoperatively. This change was analyzed using a dependent t-test for repeated measures. The secondary outcome measures were the incidences of recurrent formation of VID within 12 months of surgery and adverse events within 12 months of surgery. Of the 339 patients initially included in our study, 107 were selected. Patients who were under the age of 18 or had a history of proliferative diabetic retinopathy, vitreous hemorrhage, floaters, endophthalmitis, or ocular trauma were excluded.

CONCLUSIONS
While vitrectomy may significantly improve visual acuity for most patients with VID, recurrence and complications may occur. Limitations to this study include a small study size and limited postoperative visual acuity data.

MENTOR / DEPARTMENT
Dr. Franco Recchia, MD
Department of Ophthalmology and Visual Sciences

MDMA AND THE ANTERIOR CORTEX

OBJECTIVES
We used functional magnetic resonance imaging (fMRI) to assay motor task performance-associated brain activation changes in MDMA and non-MDMA users.

MATERIALS AND METHODS
Twenty-four subjects (14 MDMA users and 10 controls) performed an event-related motor tapping task (1, 2 or 4 taps) during fMRI at 3 T. The ACC was used to measure percent signal change (PSC) and percent activated voxels (PAV).

CONCLUSIONS
We conclude that this increase in activation with increasing MDMA use as a shift in cortical excitability, that is, the brain becomes hyper-excitible due to loss of serotonin inhibition. This evidence is consistent with MDMA-induced alterations in basal ganglia-thalamocortical circuit neurophysiology and is potentially secondary to neurotoxic effects on 5-HT signaling.

CONCLUSIONS
It is critical to understand how the brain is altered by MDMA exposure and this shift in cortical excitability may be relevant to understanding the mechanisms of action of this widely used drug.

BACKGROUND PROBLEM
In the United States, atrial fibrillation is the most common tachyarrhythmia and is becoming increasingly prevalent as the population ages. Some forms of familial atrial fibrillation are known to be associated with specific gene mutations whose products regulate the cardiac action potential. Understanding the pathophysiology of AF requires a detailed knowledge of the molecular and electrical properties of atrial myocyte activation and propagation.

OBJECTIVES
We conclude that this increase in activation with increasing MDMA use as a shift in cortical excitability, that is, the brain becomes hyper-excitible due to loss of serotonin inhibition. This evidence is consistent with MDMA-induced alterations in basal ganglia-thalamocortical circuit neurophysiology and is potentially secondary to neurotoxic effects on 5-HT signaling.

MATERIALS AND METHODS
We used functional magnetic resonance imaging (fMRI) to assay motor task performance-associated brain activation changes in MDMA and non-MDMA users.

CONCLUSIONS
We conclude that this increase in activation with increasing MDMA use as a shift in cortical excitability, that is, the brain becomes hyper-excitible due to loss of serotonin inhibition. This evidence is consistent with MDMA-induced alterations in basal ganglia-thalamocortical circuit neurophysiology and is potentially secondary to neurotoxic effects on 5-HT signaling.

CONCLUSIONS
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CONCLUSIONS
MATLAB Simulink data analysis is pending.

ACKNOWLEDGEMENTS
PhysioNet, MIT NIBIB (MATLAB PhysioNet Toolbox); Jon Peterson and David Kynor, Creare, Inc. (Intracardiac Atrial Fibrillation Database)

MENTOR / DEPARTMENT
Robert Abraham, MD, Division of Cardiovascular Medicine

THE INCIDENCE OF CATHETER RELATED BLOODSTREAM INFECTIONS IN NEONATES FOLLOWING REMOVAL OF PERIPHERALLY INSERTED CENTRAL VENOUS CATHETERS

MICHAEL CASNER
PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Previous studies examining the incidence of systemic bacterial infections following peripherally inserted central venous catheter (PICC) removal in neonates are equivocal. Because of this, clinicians often rely on anecdotal evidence in determining whether or not to prescribe prophylactic antibiotics preceding PICC removal in infants. To address this problem, we performed a retrospective cohort study to determine if PICC removal was an independent risk factor for bloodstream infections in neonates.

OBJECTIVES
To determine if PICC removal is an independent risk factor for bloodstream infections in neonates.

MATERIALS AND METHODS
A retrospective cohort of all infants admitted to the Vanderbilt Children’s Hospital Neonatal Intensive Care Unit (NICU) during 2007-2009 was analyzed with a goal of examining 1800 incidences of PICC removals. PICCs were excluded if placed outside of the NICU; if removed in another unit after more than 48 hours following transfer to another unit; if another central line was present at time of PICC removal; if a second PICC was placed within 48 hours following the original PICC removal; and if the infant was discharged or died with PICC in place. Data was collected regarding patient demographics and diagnoses as well as data regarding other infections, nature of feedings, and delivery of antibiotics during the PICC indwell period. Presence of sepsis following PICC removal was determined by a positive blood culture or by clinical treatment within 72 hours of PICC removal. Incidence of sepsis evaluations and episodes of apnea and bradycardia following PICC removal were also examined. A REDCap online database was created for data collection and statistical evaluation.

CONCLUSIONS
Conclusions not available at time of submission.

MENTOR / DEPARTMENT
Hendrik Weitkamp, MD, Department of Pediatrics

UNIQUE THREE-REGION PERFUSION STRATEGY FOR AORTIC ARCH RECONSTRUCTION

BEN W. DESCHNER
PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Aortic arch reconstruction is a necessary component of many repairs for congenital heart surgery, including the Norwood procedure. The goal of the repair is to relieve the physical obstruction while minimizing collateral physiologic burden to both the cerebral and splanchnic circulation. While early arch reconstructions were performed using deep hypothermic circulatory arrest, over the last decade an increasing volume of literature has elucidated the cognitive and neurodevelopmental benefits of selective low-flow cerebral perfusion at moderately hypothermic temperatures as opposed to complete deep hypothermic arrest. However, less advancement has been made regarding protection of the somatic viscera. Current methods presume moderate subdiaphragmatic circulatory support from collateral flow secondary to low-flow cerebral perfusion via the innominate artery. This collateral flow has been shown to provide only partial somatic circulatory support, however, and strategies for attaining such aims remain limited. We describe a simplified strategy toward optimal selective perfusion of the cerebral, splanchnic, and coronary circulations during neoaortic arch reconstruction. We postulate that this strategy may result in decreased coronary and splanchnic ischemic times with comparable postoperative hemodynamics and outcomes.

OBJECTIVES
Retrospectively compare and analyze markers of cerebral, renal, splanchnic, and coronary injury and hemodynamics between the three-region and standard perfusion strategy.

MATERIALS AND METHODS
Retrospective evaluation of charts.

CONCLUSIONS
Data not yet analyzed but will be by presentation.

MENTOR / DEPARTMENT
David Bichell, Department of Pediatric Cardiothoracic Surgery Brett Mettler, Department of Pediatric Cardiothoracic Surgery
PREVALENCE AND RISK FACTORS FOR DELIRIUM IN CRITICALLY ILL CHILDREN

STACEY DORAN

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Children have disturbances of cognition during critical illness. The clinical features of delirium within the pediatric intensive care unit (PICU) have been well-documented, but the prevalence has not been well described. It is currently unknown what risk factors predict delirium in the PICU or if these factors can be modulated to prevent its development.

OBJECTIVES
To identify the prevalence of delirium in children hospitalized in the PICU, and investigate likely risk factors for delirium development such as severity of illness, length of PICU stay, psychoactive medications, and co-morbid neurological diagnoses.

MATERIALS AND METHODS
This study is a prospective cohort study of patients aged 5 to 17 years admitted to a university-based pediatric intensive care unit who met one or more of the following inclusion criteria: mechanical ventilation, vasopressors/inotropes, Pediatric Risk of Mortality (PRISM) score over 15, or a neurological admission diagnosis. Exclusion criteria included developmental delays and non-English speaking patients or patient guardians. Delirium was diagnosed using the Pediatric Confusion Assessment Method for Intensive Care Unit (pCAM-ICU), a validated tool assessing cognitive status in the PICU. Data on risk factors were taken directly from patient electronic medical charts.

CONCLUSIONS
Critically ill children may be at an increased risk of developing delirium. It is important to determine the prevalence of delirium and identify the risk factors for the development of this condition. The potential for early therapeutic intervention and prevention of delirium needs to be explored.

ACKNOWLEDGEMENTS
Daniel Fishman, Jenna Sopfe, Dr. Pratik Pandharipande, Dr. Heidi Smith

MATERIALS AND METHODS
Fifteen obese participants and fifteen matched controls performed four trials each of the MID task while in the fMRI scanner. On incentive trials, participants could win or avoid losing money by correctly responding to the target. After each trial, feedback was presented and the participants were informed they would be paid the amount won during the task. Images were acquired on a 3T scanner.

CONCLUSIONS
Conclusions pending results.

ACKNOWLEDGEMENTS
Dr. Ron Cowan, Christina Di’lorio, Tristan Watkins & Vanderbilt Psychiatric Neuroimaging Program

MENTOR / DEPARTMENT
Ron Cowan, MD/PhD, Director, Psychiatric Neuroimaging Program

EXECUTIVE DYSFUNCTION IN CRITICALLY ILL PEDIATRIC PATIENTS

DANIEL FISHMAN

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Although significant research is occurring into the associations between adult critical illness, delirium, and long-term cognitive impairment (LTCI), in the pediatric field relatively little is known about the prevalence and predictors for LTCI or similar negative psychiatric outcomes like Post Traumatic Stress Disorder (PTSD).

OBJECTIVES
We hypothesized that critically ill pediatric patients will demonstrate executive dysfunction and PTSD 3 months after discharge from the pediatric intensive care unit (PICU), relative improvement by 6 months post-discharge. The study will test this by determining the prevalence and progression of LTCI and PTSD in patients discharged from the PICU, as well as any compounding effects between these two outcomes.
MATERIALS AND METHODS
This 2 year prospective cohort study consisted of patients ages 5 – 17 in the PICU who were also characterized by one of the following criteria: A Pediatric Risk of Mortality score of 15 or greater, mechanical ventilation, a neurological admission, or use of an inotrope or vasopressor. Patients were excluded if they were developmentally delayed before their admission or if they or their parents were non-English speakers. During admission, a parent of each patient was interviewed using the Behavior Rating Inventory of Executive Function (BRIEF) to establish baseline executive function. They were then interviewed again at 3 and 6 months post-discharge to measure LTCI. The patients were themselves assessed using the Child PTSD Symptom Scale and Self-BRIEF during the follow-up interviews if they were above the ages 7 and 11 respectively.

CONCLUSIONS
Identifying the prevalence and predictors of LTCI and PTSD among pediatric patients is an early and critical step in increasing hospitals’ ability to minimize these negative outcomes.

ACKNOWLEDGEMENTS
Stacy Doran, Jenna Sopfe, Pam Berry, Matt Kynes

MENTOR / DEPARTMENT
Ronald Cowan, Psychiatry

HIPPOCAMPAL AND AMYGDALA VOLUMES IN EUTHYMIC BIPOLAR I PATIENTS
ALANA LEWIS

BACKGROUND PROBLEM
Abnormalities of the hippocampus and amygdala have been implicated in the pathophysiology of bipolar disorder. However, research examining the hippocampus and amygdala in bipolar disorder has been inconsistent in demonstrating volumetric differences in these limbic structures.

OBJECTIVES
The present study examined hippocampal and amygdala volumes between patients with bipolar disorder and matched healthy controls.

DEVELOPING NOVEL CEREBROVASCULAR METRICS TO PREDICT INTRACRANIAL ANEURYSM RUPTURE: DOES SIZE RATIO MATTER?
DENNIS TIMOTHY LOCKNEY

BACKGROUND PROBLEM
The usage of the recreational drug Ecstasy, also known as methylenedioxymethamphetamine (MDMA) has increased in the number of “past year initiates” according to the NSDUH (National Survey on Drug Use and Health). Reports in animal models have consistently shown serotonin neurotoxicity.

CONCLUSIONS
We hypothesize that MDMA can cause structural changes in the cortex of the brain and we want to be able to quantitate the effects.

MATERIALS AND METHODS
Euthymic patients with Bipolar disorder, type I, and matched healthy control participants were included in the study. Volumetric estimates of the right and left hippocampus and amygdala of each participant were obtained by manually tracing the structures following a three-dimensional morphometric protocol on high resolution structural magnetic resonance images (MRI). The right and left hippocampal volumes were additionally segmented into anterior and posterior subregions.

CONCLUSIONS
Results from the current study did not identify hippocampal or amygdala volumetric differences in bipolar patients. However, different relationships between hippocampal and amygdala volumes across the groups were detected. Furthermore, significant relationships between clinical factors and hippocampal and amygdala volumes in the current study suggest that variability in research samples of bipolar populations may contribute to the equivocal research examining volumetric differences. Further studies are needed to examine how clinical factors may affect hippocampal and amygdala volumetric estimates in bipolar disorder.

ACKNOWLEDGEMENTS
Austin Woolard, Alyssa Birmingham

MENTOR / DEPARTMENT
Dr. Jo Cara Pendergrass, Department of Psychiatry

VANDERBILT UNIVERSITY SCHOOL OF MEDICINE - EMPHASIS PROGRAM - FORUM VI - MAY 2011
BACKGROUND PROBLEM
Determining the best predictor of intracranial aneurysm (IA) rupture has caused significant controversy. The International Study of Unruptured Intracranial Aneurysms (ISUIA) determined that aneurysms less than 7 mm in size have a very small risk of rupture over five years, and that treatment of small IAs posed more risk than conservative therapy, and should be avoided. However, experienced surgeons agree that these IAs have a greater risk of rupture than the ISUIA findings suggest. Disagreement between experience and the ISUIA study has resulted in exploring new metrics that better predict rupture than size alone. Our study focused on developing the Aneurysm to Vessel Ratio (AVR) parameter to better predict rupture.

OBJECTIVES
Disagreement between experience and the ISUIA study has resulted in exploring new metrics that better predict rupture than size alone. Our study focused on developing the Aneurysm to Vessel Ratio (AVR) parameter to better predict rupture.

MATERIALS AND METHODS
A retrospective study involving 203 patients was conducted in which researchers measured aneurysmal parameters and cisternoscleral diameters from rotational two-dimensional computed tomography angiography. Ninety-nine patients had aneurysmal sub-arachnoid hemorrhages and 104 patients had unruptured aneurysms. The AVR was calculated by dividing the aneurysm size by the normalized parent artery diameter. A 2-tailed Mann-Whitney statistical test was performed to assess statistical significance between ruptured and unruptured aneurysms located distal to the dural ring.

CONCLUSIONS
The aneurysm to vessel ratio is a promising new metric to predict aneurysm rupture. AVR is easily calculated from measurements from two-dimensional computed tomography angiography scans. Our study indicates that AVR better predicts rupture status than size of the aneurysm, and that guidelines based on the ISUIA report should be reevaluated.

ACKNOWLEDGEMENTS
Maysan Ghiassi

MENTOR / DEPARTMENT
Robert Mericle M.D.

INTRAOPERATIVE SKIN CONDUCTANCE CHANGES DURING PROCESSING OF EMOTIONAL STIMULI IN PARKINSON’S DISEASE

NEIL MANUS

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Emotional processing is affected during the course of Parkinson’s disease, but the neural substrates of this change are unknown. Models suggest that there are parallel motor, cognitive and affective circuits that flow from cortex to basal ganglia through the thalamus and back to cortex. There is evidence that the subthalamic nucleus (STN) and other basal ganglia nuclei have direct and indirect influences from frontal and limbic cortex (Temel 2005).

OBJECTIVES
Our goal was to test the hypothesis that emotional stimuli are processed in the basal ganglia. We tested whether skin conductance (SC) can be used as an independent measure of emotional reaction other than the patient’s self-report. While SC is an established method for measuring affective reaction, we tested whether it can be used in the context of Deep Brain stimulation (DBS) surgery.

MATERIALS AND METHODS
During DBS surgery emotional pictures or music were used to evoke emotional changes in the patient. We attached SC electrodes to the anterior intermediate phalanx which was connected to the Biopac MP150 recording system. The team waits 5-10 minutes for electrodes to acclimate to the skin and for the electrophysiologist to find active neurons in the STN. In the picture protocol, the International Affective Picture System is used to display 50 prescreened one-second long random-order pictures. In the music protocol, 9 custom thirty-second long music clips are played for patients, after which they rate for valence and arousal on a 1-10 scale. In addition, we measured SC during this period. To control for overall effects of surgery on SC to emotional stimuli, we also measured SC in pre-operative DBS patients, patients undergoing stimulation of the sensory thalamus for essential tremor treatment, and in healthy controls.

CONCLUSIONS
Our long-term goal is to correlate changes in emotional arousal in patients undergoing DBS surgery with neuronal activity in the STN.

ACKNOWLEDGEMENTS
Corrie R. Camalier, PhD Laura Allen, BE

MENTOR / DEPARTMENT
Joseph Neimat, MD, Department of Neurosurgery

HOST GENETIC VARIATION IS ASSOCIATED WITH THE DEVELOPMENT OF CANCER METASTASIS

DEVIN PATEL

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
The mechanisms by which metastatic cells arise from primary tumors depend not only on the particular cancer cells involved, but also on the host-specific genetic variations. Identification of these genetic variations would increase our ability to identify and treat patients at high risk of systemic disease.

OBJECTIVES
We hypothesized that by using large scale genome analysis, we could
identify single nucleotide polymorphisms (SNPs) that increase the likelihood of developing metastatic disease.

**MATERIALS AND METHODS**
A case population of 300 patients who had metastatic cancer and a control population of 717 patients who had cancer but did not develop metastatic disease was defined. These two populations were matched so that they had similar median age, median follow-up time, gender, race and primary cancer site distribution. A retrospective case-control association study at 115 SNPs was performed.

**CONCLUSIONS**
Host genetic variations contribute to the development of cancer metastasis. The identification these variations may help distinguish patients who have a high risk of developing systemic disease from those at a lower risk. We are currently validating whether the SNPs identified in this study can be used to predict which patients are more likely to develop systemic disease.

**ACKNOWLEDGEMENTS**
JM Alvarez, Y Shyr, AB Chakravarthy, F Xia

**MENTOR / DEPARTMENT**
Anuradha Chakravarthy-Radiation Oncology

**ACTIVE VITAMIN D3 (VITD) ADMINISTRATION AND INSULIN RESISTANCE IN CHRONIC HEMODIALYSIS (CHD) PATIENTS**

**NATALIA PLOTNIKOVA**
PATIENT ORIENTED RESEARCH

**BACKGROUND PROBLEM**
Active vitamin D administration in CHD patients has been the mainstay to control secondary hyperparathyroidism. However it has been recently recognized that Vitamin D deficiency is linked to increased cardiovascular risk both in the general population and in CHD patients. One of the postulated metabolic mechanisms implicated in the increased risk include its effects on insulin resistance (IR).

**OBJECTIVES**
To determine the effects of 1,25-Dihydroxyvit D3 administration on CHD patients while on a background of Cinacalcet to control PTH on chronic inflammation, Insulin sensitivity and adipocytokines.

**MATERIALS AND METHODS**
In a pilot double blinded randomized clinical trial, 10 prevalent CHD patients (52.9 years old, 100% African American, 33% females, 33% with history of diabetes, body mass index 34.8 kg/m2) on stable VitD treatment were taken off their VitD for 8 weeks. iPTH levels were kept at baseline levels (within 10%) by administration of Cinacalcet as needed. At the end of 8 weeks, patients were randomly assigned to continue Cinacalcet or to restart an active vitamin D analog. The primary outcome was insulin resistance assessed by glucose disposal rate (GDR) measured by hyperinsulinemic euglycemic clamp (HEGC). Other important measures included other indirect indices of IR and serum adipokines.

**CONCLUSIONS**
This study showed no effect of Vitamin D on IR measured by HEGC or on inflammatory markers while on a background of Cinacalcet.

**ACKNOWLEDGEMENTS**
Mary B. Sundell, Aihua Bian, Ayumi Shintani, PhD, Edward Siew, MD, Charles D Ellis, PhD

**MENTOR / DEPARTMENT**
Dr. Ikizler, Vanderbilt Department of Nephrology; Dr. Hung, Vanderbilt Department of Nephrology

**PERCEPTIONS OF FUNCTIONING AND AWARENESS OF DEFICITS POST-CRITICAL ILLNESS IN ICU SURVIVORS**

**MEERA REDDY**
PATIENT ORIENTED RESEARCH

**BACKGROUND PROBLEM**
Data suggest that intensive care unit (ICU) survivors suffer from objective neuropsychological and emotional impairments. However, questions remain regarding how individuals view their own post-ICU functioning as well as the accuracy of their self-perceptions.

**OBJECTIVES**
To characterize the self-perceptions of ICU survivors regarding daily functioning after critical illness, to determine the relationships between their perceptions and the perceptions of surrogates, and to identify risk factors associated with functional decrements after critical illness.

**MATERIALS AND METHODS**
Subjects were adult medical ICU (MICU) patients who were assessed at 3 and 12 months post-ICU discharge with the Awareness Questionnaire (AQ), a 17-item assessment (patient and surrogate versions), comprised of items pertaining to awareness of cognitive, behavioral-affective, and motor-sensory functioning. Subjects were additionally evaluated with a neuropsychological battery.

**CONCLUSIONS**
ICU survivors had accurate awareness of deficits, as reflected in the fact that their self-reports were similar to those of their surrogates. A significant majority of ICU survivors function at levels “a little worse” or “much worse” than baseline after critical illness and experience difficulties in behavioral/affective, motor-sensory, and cognitive domains, despite the fact that research to date has identified cognitive problems as primary. Patients do not report meaningful
improvements in global or domain specific functioning from 3 months to 12 months after hospital discharge. Future investigations should focus on identifying modifiable risk factors associated with perceived functional decline.

Acknowledgements
Dr. James Jackson, Dr. Mario Davidson, Dr. Wes Ely

Mentor / Department
Dr. James Jackson and Dr. Wes Ely

MINIMUM CLINICALLY IMPORTANT DIFFERENCE IN PAIN AFTER MICROVASCULAR DECOMPRESSION FOR TRIGEMINAL NEURALGIA
VISHRUTH K REDDY
PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Outcome studies rely on patient reported outcome (PRO) measurements to assess treatment effectiveness but can lack direct clinical meaning. The concept of minimum clinical important difference (MCID) has been utilized to measure the critical threshold needed to achieve clinically relevant treatment effectiveness and remains uninvestigated for microvascular decompression (MVD), a treatment for trigeminal neuralgia (TN).

OBJECTIVES
We set out to determine the most appropriate MVD-specific MCID values for pain improvement with respect to Visual Analog Scale (VAS) and Barrow Neurological Institute (BNI) pain scale.

MATERIALS AND METHODS
In 38 consecutive patients undergoing MVD for TN, PRO measures of pain (VAS, BNI pain scale) were prospectively assessed pre-operatively and one year post-operatively. Four well-established, anchor-based MCID calculation methods were utilized to calculate MCID [average change; minimum detectable change (MDC); change difference; receiver operating characteristic (ROC) curve analysis] for three separate anchors [health transition index (HTI) of the Short Form-36; satisfaction index; willingness to have surgery again].

CONCLUSIONS
In this patient population, the MDC approach with the SF-36 HTI anchor appears to be the most appropriate method for calculating MCID thresholds, as it provided a threshold above the 95% confidence interval of the un-improved cohort (greater than the measurement error) and was closest to the mean change score reported by improved patients, with thresholds at 9.4 points for VAS and 3.6 points for BNI pain scale.

ACKNOWLEDGEMENTS
Scott L Parker, The Johns Hopkins University School of Medicine; Samit A Patrawala, Vanderbilt University School of Medicine

MENTOR / DEPARTMENT
Robert A Mericle, MD Department of Neurological Surgery

LARGER AMYGDALA VOLUME AS A BIOLOGICAL MARKER FOR INHIBITED TEMPERAMENT
APRIL SEAY
PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Temperament refers to biologically-based differences in mood, emotions, and behavior. One dimension of temperament is how a person responds to new and unfamiliar situations. Inhibited individuals avoid novelty whereas uninhibited individuals typically approach novelty. Inhibited and uninhibited are the two extremes that describe approach to novelty. Inhibited temperament is a risk factor for anxiety disorders, and the amygdala has been implicated as an important neural substrate. Using functional magnetic resonance imaging (fMRI), previous studies have shown differences in amygdala function between inhibited and uninhibited individuals.

OBJECTIVES
The purpose of this study was to explore whether structural differences underlie the observed functional differences between inhibited and uninhibited individuals.

MATERIALS AND METHODS
92 individuals (ages 18-40 years) with either extreme inhibited (n=46) or uninhibited (n=46) temperament both as children and adults participated in the study. Structural MRI images were collected on a 3T scanner. To assess volume, the amygdala and hippocampus were manually segmented using 3D Slicer 3.4 following standardized protocols. Temperament group differences in amygdala and hippocampus volume were tested using analysis of variance with age, gender, handedness, and race as covariates.

CONCLUSIONS
This study demonstrates there are structural differences in the amygdala between inhibited and uninhibited individuals. This study provides initial evidence for a structural basis to the previously observed functional amygdala differences in individuals with an inhibited temperament. Increased amygdala volume may contribute to the higher incidence of anxiety disorders seen in inhibited temperament, and these differences could correlate to risk factors for anxiety.

ACKNOWLEDGEMENTS
Dr. Jennifer Blackford, Ross VanDerKlok

MENTOR / DEPARTMENT
Dr. Jennifer Blackford, Vanderbilt University Psychiatric Neuroimaging Program, Department of Psychiatry
AVOIDANCE OF SUNLIGHT EXPOSURE IN HEMATOPOIETIC CELL TRANSPLANT PATIENTS: EFFECT ON VITAMIN D LEVELS AND BONE TURNOVER MARKERS

CRAIG A. SHEEDY

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM

Survivors of hematopoietic cell transplant (HCT) are at risk for a number of adverse health outcomes, including low bone mineral density (BMD). Low BMD is predictive of fracture risk, increased non-cause specific mortality, and cardiovascular mortality in adults. Factors contributing to low BMD include pharmacologic glucocorticoid use for immunosuppression and low serum 25-hydroxyvitamin D due to decreased physiological production and absorption from dietary sources.

OBJECTIVES

The specific aims of this study are to 1) determine the prevalence of vitamin D insufficiency/deficiency in patients during the first year post-transplant; 2) identify host, dietary, and environmental risk factors for vitamin D insufficiency/deficiency; and 3) identify abnormalities in bone turnover and associations with vitamin D insufficiency/deficiency.

MATERIALS AND METHODS

This prospective longitudinal cohort study follows pediatric participants receiving a HCT from baseline to one year post-transplant. Baseline data includes serum and urine markers of vitamin D status and bone turnover, DEXA scan, and food frequency and sunlight exposure questionnaires. Lab data and questionnaires are recollected at day 100 post-transplant, and at six-, nine-, and 12-month follow-up appointments. In addition, one hundred pediatric control participants are enrolled to provide normative data for comparison with HCT participants.

CONCLUSIONS

HCT patients have lower 25-hydroxyvitamin D levels at transplant than healthy children, and are less likely to report taking vitamin supplementation. Serum 25-hydroxyvitamin D levels show seasonal variation and are lowest in spring.

ACKNOWLEDGEMENTS

Elizabeth Koehler, Biostatistician III- Division of Cancer Biostatistics; Haydar Frangoul, M.D., Pediatric Hematology/Oncology; Jada Meriwether, Clinical Trials Associate II; Jennifer Domm, M.D., Pediatric Hematology/Oncology; Rebecca Manes, RN, MSN Pediatric Hematology/Oncology; Vanderbilt Division of General Pediatrics. Funding provided by Vanderbilt Institute for Clinical and Translational Research (VICTR).

MENTOR / DEPARTMENT

Jill Simmons, M.D., Department of Pediatrics- Ian M. Burr Division of Pediatric Endocrinology and Diabetes

CONSTRAINT-INDUCED MOVEMENT THERAPY IMPROVES NEURAL PROCESSING AND NEUROBEHAVIORAL FUNCTION IN CHILDREN WITH CEREBRAL PALSY

ASHLEY SIMMONS

PATIENT ORIENTED RESEARCH

BACKGROUND PROBLEM

Cerebral palsy (CP) is a non-progressive disorder of movement for which there exist few evidence-based therapies. The incidence of cerebral palsy (CP) in the US is 2-3/1000 infants born, and every year approximately 240 new cases are diagnosed in TN. Yet, few evidence-based therapies exist to treat CP. Constraint-Induced Movement Therapy (CIMT) holds promise as an effective treatment for CP but suffers from a wide variation in treatment regimens and lack of objective measurement tools. Multimodal assessments can help optimize the length of treatment, the type of constraint and the exercise content of future CIMT interventions.

OBJECTIVES

To combine neurobehavioral, electrophysiological and neuroimaging assessments to quantify the effect of constraint-induced movement therapy (CIMT) on neural and behavioral function.

MATERIALS AND METHODS

Prospective study of a 1-week intensive camp of CIMT in 11 children (5-12 years) with hemiparetic CP associated with neonatal brain lesions. Constraint was worn continuously for one week in group and individual OT/PT settings with motor and sensory tasks. Standardized neurobehavioral and sensory assessments of upper extremity function were correlated with latency and amplitude of event-related potentials (ERPs) in response to two established paradigms targeting speed and efficiency of brain processing.

CONCLUSIONS

CIMT had a strong positive effect on neurobehavioral and neurocognitive function and the two were often correlated. ERP measures showed greater increases in processing speed in children with left-sided brain lesions, with shorter latencies on the side contralateral to the lesions after CIMT. Neurobehavioral assessments can be combined with ERP to quantify improvements in neural function after CIMT. This systematic approach to the effect measurement holds promise for evidence-based therapy design in children with CP. To assess for persistence of effects, neurobehavioral and ERP testing have been repeated 6 months post-CIMT. We will correlate ERP and neurobehavioral measurements with motor and sensory tasks. Continuous neuroimaging assessments to quantify the effect of constraint-induced movement therapy (CIMT) on neural and behavioral function.

ACKNOWLEDGEMENTS

Dr. Nathalie Maitre, Sasha Key, Vanderbilt Children’s Rehabilitation Center Therapist, The National Institutes of Health, Vanderbilt IRB, Vanderbilt Medical School Emphasis Program.
**BACKGROUND PROBLEM**

Dysregulation of the coagulation cascade and pathologic thrombosis complicate a variety of diseases. They represent significant sources of morbidity and mortality in both chronic diseases, such as diabetes and lupus, and acute illness, such as infection and trauma. However, current clinical measures of coagulation are much better at detecting hypercoaguable states than hypercoaguable states - which put patients at risk for pathologic thromboses.

**OBJECTIVES**

Many chronic diseases can cause increased levels of thrombin generation than measured in controls but, due to the variability within the general population, this difference is not large and may not be significant. However, orthopedic surgery patients generate significantly higher levels of thrombin generation which differ dramatically from the general population. Therefore, we hypothesize that thrombin generation has the potential to be a useful tool to provide meaningful information regarding hypercoaguableity in orthopedic patients. As a proof of concept, we sought to determine whether hyper or hypocoaguable as measured by the thrombin generation assay corresponded with or could predict adverse events of dysregulated coagulation.

**MATERIALS AND METHODS**

We performed retrospective observational case studies of the patient plasma and compared it to their clinical course. Inclusion criteria included Vanderbilt adult orthopedic patients who had undergone total hip or knee arthroplasty, or spinal surgery. We used the thrombin generation assay (TGA) to measure procoagulant activity of the plasma as indicated by thrombin generation levels. We also measured thrombin generation after addition of protac (a protein C activator) and low molecular weight heparin (an anti-thrombin III activator), thus providing a measure anti-coagulant capacity of the plasma. Thrombin levels were charted pre-operatively and up to five days post-operatively and compared to star panel records of adverse events including thromboembolic events, or hypo-coaguable events such as hematoma. Additionally, we compared deep vein thrombosis prophylaxis regiments to determine the levels of thrombin generated produced on the different medication regimens.

**CONCLUSIONS**

The thrombin generation assay has the potential for measuring clinically relevant hypercoaguableity in acute settings such as trauma and surgery. However, it is less clinically useful for hypercoaguableity associated with chronic diseases. Future studies are needed to determine a “safe” range of thrombin generation, and to specifically define the levels of thrombin generation that put patients at risk for adverse bleeding or clotting events.

**ACKNOWLEDGEMENTS**

Dr. Jon Schoenecker, Lynda O’Rear

**MENTOR / DEPARTMENT**

Dr. Jon Schoenecker, Department of Pharmacology

**111In-DOTATATE RADIOPROBE GUIDED THORACOSCOPIC LOCALIZATION OF LUNG CANCER**

**FRANCYS C. VERDIAL**

**PATIENT ORIENTED RESEARCH**

**BACKGROUND PROBLEM**

Lung cancer is the number one cancer killer. The only proven means of curing patients with lung cancer is via early diagnosis and resection, an improved means of intraoperative localization of small, nonpalpable nodules would allow resection of these nodules by minimally invasive techniques, which are safer and more cost-effective.

**OBJECTIVES**

We hypothesize that a radiolabeled somatostatin analog will permit intraoperative localization of nonpalpable lung nodules. We determined the biodistribution characteristics of 11In-DOTATATE during intra-operative resection of solitary pulmonary nodules in ten patients with 1.5 to 3.0 cm biopsy-proven non-small cell lung cancer (NSCLC).

**MATERIALS AND METHODS**

Four patients aged 40-89 years with newly diagnosed untreated primary lung cancer of the upper lung fields with a CT diameter of 0.5 – 4.0 cm were identified through the Nashville VA pulmonary nodule clinic or the Thoracic Surgery Clinic. Patients were injected with 2.7-3.17 µCi of 11In-DOTATATE and underwent a SPECT/CT within 4-24 hours and thoracoscopic upper lobectomy 20-91 hours later. In the operating room, the lung tissue thought to contain the nodule was examined with an intraoperative gamma probe intraoperatively and postoperatively, to quantify the degree of uptake in the nodule and determine if the probe can successfully discriminate between the lung cancer and noncancerous lung. Resection and pathological examination was performed according to standard of care.

**CONCLUSIONS**

Preliminary results are promising, suggesting a use for 11In-DOTATATE in intraoperative localization of lung nodules. The data elucidates problem areas that must be addressed prior to completing data collection.
Attempts will be made to maximize the lesion/lung ratio, by improving the shielding on the probe, minimizing background, and increasing the lesion signal. We are in the process of increasing the injection-to-scan and injection-to-operation time to allow for increased washout and, thus, decreased background activity. Similarly a higher dose of 111In-DOTATATE will be utilized to increase the signal. The protocol followed for subsequent patients will exhibit these modifications.

ACKNOWLEDGEMENTS
Dr. Jamii St. Julien, Dr. Ron Walker, Stephen Deppen

MENTOR / DEPARTMENT
Dr. Eric L. Grogan, Thoracic Surgery

SHORT-TERM EFFECT OF PHYSICIAN DISCUSSIONS AND AN EDUCATIONAL INTERVENTION ON CHILDREN’S HABITS RELATED TO A HEALTHY WEIGHT
MARGARET (MOLLY) WHITE
PATEIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
It is unknown if interventions during the primary care visit can affect children’s habits related to reaching or maintaining a healthy weight.

OBJECTIVES
To determine if parent-physician discussions and a brief primary care intervention can affect children’s habits related to reaching or maintaining a healthy weight.

MATERIALS AND METHODS
English and Spanish speaking caregivers of children aged 2 to 12 presenting to a pediatric primary care clinic for a well child visit were randomized (n=219) to an 8 minute multimedia intervention or control at triage (1:1 ratio). A Spanish translation of the program was provided for Spanish speaking caregivers. Caregivers were invited to participate in a study that included a 2 week follow up phone call. The follow up phone call survey was completed with 156 (71.2%) caregivers.

CONCLUSIONS
Physician discussions and multimedia interventions can have a short term affect on children’s habits related to reaching and maintaining a healthy weight. These results have implications for how to incorporate routine anticipatory guidance about obesity prevention into the primary care visit.

ACKNOWLEDGEMENTS
Jill Aragon, Antwon Chavis, Julia Hudnut-Beumler, Mary Dietrich, PhD

MENTOR / DEPARTMENT
Seth Scholer, Vanderbilt Department of Pediatrics

M. T. PH. D.

CONCLUSIONS
Mothers colonized with S. aureus, regardless of site of carriage, are more likely to have newborns that are also colonized with S. aureus. The data suggests that while vertical transmission may occur, horizontal transmission from a variety of potential sources plays a significant role in newborn carriage.

ACKNOWLEDGEMENTS
Buddy Creech, MD, MPH; Natalia Jiménez; Elizabeth Saye, Andrew Alsentzer

MENTOR / DEPARTMENT
Buddy Creech, MD, MPH Division of Pediatric Infectious Disease

STAPHYLOCOCCAL COLONIZATION IN WOMEN AND NEWBORNS
JESSE WRIGHT
PATEIENT ORIENTED RESEARCH

BACKGROUND PROBLEM
Staphylococcus aureus (S. aureus) is a ubiquitous microorganism occupying the anterior nares of nearly one-third of the human population at any time. S. aureus has re-emerged as a significant neonatal pathogen and maternal-infant (M/I) transmissibility has not been fully elucidated.

OBJECTIVES
To determine if neonatal colonization of S. aureus occurs vertically, at the time of delivery, or occurs as a result of horizontal transmission in the days and weeks following birth.

MATERIALS AND METHODS
629 expecting mothers were enrolled into the study during their prenatal visits (weeks 30-38). On day of delivery, 473 women were tested for S. aureus colonization by nasal or vaginal swabs. Newborns received both nasal and umbilical swabs on the day of delivery. M/I pairs received subsequent nasal swabs at the time of hospital discharge and during 2 and 4 month follow-up visits. S. aureus cultures were genotyped to determine relatedness of M/I strains.
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