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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’ areas 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 nine Emphasis focus areas in which students can choose projects: Biomedical Informatics, Community Health Initiatives and Health Outreach, Global Health, Healthcare and Public Health Research and Management, Laboratory-Based Biomedical Research, Law and Policy, Medical Education, Medical Humanities, and Patient-Oriented Research. Students choose their areas, mentors and projects during the fall semester of first year, 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 summer between 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 a part of our Medical School 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 the research areas that will lead to 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 the projects carried out by the Class of 2011. The broad range of projects reflects the diversity of interests our students bring with them to medical school. We are tremendously proud of their accomplishments and hope that this experience has been a rewarding first step on the path to leadership and scholarship.
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, both in terms of 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 the interviewing summer. As Director of the Emphasis Program, I want to express my thanks to those who willingly accepted the responsibility of mentoring these students. The quality of the work reported in this volume is evidence of the effectiveness of this collaboration.

These 104 abstracts represent 14 oral presentations and 83 posters that were presented at the Emphasis Forum at Vanderbilt University School of Medicine on May 11th and 12th, 2009. Of these abstracts, 93 represent the work of students who entered the Emphasis Program in the fall of 2007. Eleven abstracts describe research performed by students in Vanderbilt’s Medical Scientist Training Program.

Consistent with the aims of the Emphasis Program, the topics covered in these 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 into the next phase of their medical education. Others may hand their projects off to the next class entering the program. Regardless of the future direction these projects take, it is clear that 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 mentor over the past 18 months has forged a relationship that will endure in the coming 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.
Cindy Gadd is an associate Professor of Biomedical Informatics. She has been the Director of Graduate Studies for Department of Biomedical Informatics graduate degree programs since January 2006 and is the Principal Investigator on our NLM Biomedical Informatics Training Grant, which was recently renewed through 2012. She is an elected Fellow of the American College of Medical Informatics and an active participant in the informatics education initiatives of the American College of Medical Informatics Association. Her primary area of research and publication is the implementation and evaluation of integrated clinical information systems, including electronic health records (EHR) systems, in large health care networks. Since joining Vanderbilt, Dr. Gadd has become a co-investigator in the evaluation of the development, deployment, and sustainability of a regional health information exchange and is co-developing ePrescribing evaluation research focused on surrogate prescribers, patients, and pharmacies.

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.”
**DEVELOPMENT AND EVALUATION OF NOVEL FEATURE SELECTION METHODS FOR HIGH DIMENSIONAL DATA ANALYSIS**

**KASSATHUN GEBRE-AMLAK**  
*Biomedical Informatics*

**Background/Problem:**  
Recent advances in biological research and information retrieval have generated large datasets which can give us insight into the biological processes and risk factors of diseases. From the fields of bioinformatics and machine learning, computational causal discovery methods are of great interest, primarily because they can be applied to elucidate causal structure from observational data, thus enhancing our ability to direct and tailor biological research questions. However, many of these methods are not scalable and/or slow when applied to the recent spate of high-throughput datasets.

**Objectives:**  
The goal of this project is to derive novel causal discovery methods that provide significant computational efficiency compared to prior techniques.

**Methods and Materials:**  
Four publicly available datasets from the domains of structural biology and information retrieval were used for development and evaluation of novel methods. These methods involve efficient data parallelization schemes and were executed on the Vanderbilt High Performance Computing Center ACRAE.

**Results:**  
Results show that for some datasets novel causal discovery methods provide significant improvement in terms of execution time compared to prior methods. However, there exist datasets where parallel algorithms do not necessarily make causal discovery faster.

**Conclusions:**  
Parallelization efficiency depends on the structure of the dataset and the parameters of parallelization. It is necessary to devise computational tools to screen large datasets in order to determine whether it is beneficial to apply prior or novel parallel algorithms for causal discovery. Such tools have a promise to reduce time of causal discovery from observational data.

**Acknowledgements:**  
Alexander Statnikov, Laura Brown, and Firas Wehbe

**Mentor(s) and Department:**  
Constantin Aliferis, Department of Biomedical Informatics, Vanderbilt University School of Medicine

**SEC FOOTBALL INJURY TRACKING DATABASE DEVELOPMENT**

**LUKE LAFFIN**  
*Biomedical Informatics*

**Background/Problem:**  
There exists a paucity of data with respect to the treatment of injuries of elite athletes. Furthermore, important clinical endpoints for elite athletes, such as return-to-play measures, are not often explored.

**Objectives:**  
This project aims to create a foundation for injury tracking among the schools of the Southeastern Conference (SEC) through the establishment of an online database to document the treatment and return-to-play outcomes of two football acquired injuries: anterior cruciate ligament ruptures and syndesmotic or high ankle sprains.

**Methods and Materials:**  
A variety of issues were considered in the database design. Most significant of these issues include the security of information due to the high profile nature of the patients, the investigators timeframe for access to the entered information, and the efficient implementation of such a system due to the great number and variety of users. A range of platforms to house the database was explored so as to best combat these issues. The REDCap software at Vanderbilt is currently the most efficacious platform on which to begin this implementation.

**Results:**  
The database is scheduled to begin collecting true patient/athlete data at the commencement of the 2009 National Collegiate Athletic Association (NCAA) football season in August 2009. Preliminary training material has been completed and implementation/training among the twelve participating institutions should begin shortly.

**Conclusions:**  
Conclusions with respect to the implementation and effectiveness of the database will be better judged upon completion of the 2009 NCAA football season.

**Mentor(s) and Department:**  
Kurt Spindler MD, Orthopaedics

**EVALUATION OF VOLUNTEER SATISFACTION AT SHADE TREE FAMILY CLINIC**

**ARTYOM SEDYKH**  
*Biomedical Informatics*

**Background/Problem:**  
Shade Tree Family Clinic (STFC) is a medical student run clinic in East Nashville that is affiliated with Vanderbilt University Medical Center. Patient services at STFC are provided by student and faculty volunteers. Few studies have examined the level of satisfaction volunteers experience at student run clinics.

**Objectives:**  
To assess volunteer satisfaction at STFC and factors contributing to it.

**Methods and Materials:**  
Volunteers were asked to complete an anonymous free-text survey to assess both positive and negative factors associated with work at STFC. Based on responses, subpopulation-tailored anonymous surveys (physician, preclinical student, and clinical student) were designed and distributed at STFC over the summer of 2007-2008 school year. All survey items were Likert scale. Statistical analysis included test of association on data stratified by overall satisfaction.

**Results:**  
Out of the total number of responses (n=61), 21% were from physicians, 31% from clinical students, and 48% from preclinical students. All of the volunteers agreed or strongly agreed (77%) that their overall experience was positive. Of those who strongly agreed that their experience was positive, 93% strongly agreed that STFC provides high quality of care (p = 0.001), 81% strongly agreed that volunteering helps students to develop a sense of responsibility (p=0.006). Other significant associations included the non-intimidating environment as being important, team enthusiasm as a motivational factor, and a sense of community.

**Conclusions:**  
It appears that all the factors associated with strongly positive experiences at STFC are most attributable to positive interpersonal interactions. These
results suggest that an environment conducive to interaction between volunteers promotes satisfaction.

Acknowledgements:
I am indebted to all STFC volunteers who have freely offered their precious assistance. I am also indebted to Mario A. Davidson, Ph.D., the biostatistician of the Emphasis Program, for his assistance with data analysis - his utter support of this project went well beyond mere professionalism. I acknowledge Robert F. Miller, M.D., for his continuous sacrificial service to the patient population of the Shade Tree Family Clinic and for his contribution to the professional development of student volunteers. Most of all, I acknowledge Trent S. Rosenbloom, M.D., who never failed to extend his wonderfully kind mentorship to me throughout this project in the most meaningful way.

Mentor(s) and Department:
Samuel Trent Rosenbloom, MD, Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, TN
Community Health Initiatives and Health Outreach embraces health issues that disproportionately affect specific populations, especially but not exclusively underserved populations of all ages. Projects and study in this area link academic medical education with community needs. Student projects address one of the following six targeted areas of study:

1. Health risks/diseases—entities that disproportionately affect undeserved populations.
2. Obstacles to health and healthcare for the underserved.
3. Socio-cultural, historical and medical aspects of caring for an underserved population.
4. The principles, approaches and skills needed by successful medical provider in an underserved community.
5. Skills and strategies that motivate patients to practice positive health behaviors.
6. Diagnosis of healthcare needs of a community and development of plans to meet those needs.

“The 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. This group of Community Health Emphasis students are brilliant, energetic, and helpful to each other every 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 cases, became award winners for service to the community.”

“They (students) 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.”

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 a therapist with children. Ms. Clinton helped develop a system of alternative health services for seniors for the state of Georgia and has served as an advisor to 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.
PREGNANCY RISK FACTORS AND HEALTH CARE CHALLENGES FOR PREGNANT LATINA ADOLESCENTS

Meredith Albin
Community Health

Background/Problem:
Adolescent pregnancy in minority populations is a significant public health concern associated with pre-term birth, low birth weight babies, and infant mortality. In Davidson County, Tennessee, approximately 164/1000 Latina teens give birth annually, four times greater than the teen national average. The investigator sought to know more about the risk factors that impact birthing outcomes for this population.

Objectives:
This study aimed to determine the pregnancy health risks, challenges, and concerns of pregnant Latina adolescents for future advocacy, outreach, and educational efforts.

Methods and Materials:
Thirteen participants aged 14-20 who were enrolled in the Latina Birthing Project (LBP) were administered a 57-item questionnaire adapted from established healthcare surveys. It addressed pregnancy planning, access to healthcare, perceived quality of care, nutrition, substance use, and abuse. Additionally, seven young women participated in a focus group addressing concerns and interventions related to pregnancy planning and abuse.

Results:
When surveyed, 23.1% participants reported being physically abused during their pregnancy while 7.6% reported continuing to feel unsafe at home. Only 20% reported being asked whether someone was hurting them during any prenatal care visit with 46.2% of respondents being classified as “food insecure” over the past 12 months, a period encompassing their pregnancy. Finally, 76.9% of the study population did not speak with anyone in preparation for the pregnancy, and 80% did not use contraception.

Conclusions:
The greatest concerns identified were pregnancy planning, nutrition, and physical abuse during pregnancy. There is capacity for the LBP to address these needs in the population. In focus group discussion, participants were receptive to supportive public health interventions and educational initiatives. Emphasis on empowerment of adolescents and creation of community is essential.

Acknowledgements:
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Mentor(s) and Departments:
Dr. Nick Desai, Department of Pediatrics, Division of Adolescent Medicine and Behavioral Science, Vanderbilt University Medical Center and Bethany Hard, Coordinator of the Latina Birthing Project, Metro Public Health Department.

COMPARING THERAPEUTIC MODALITIES FOR THE TREATMENT OF SEXUAL ASSAULT SURVIVORS

Dana Harrar
Community Health

Background/Problem:
One in four girls and one in six boys are sexually abused before the age of 18. In addition, one in six women and one in 33 men will experience attempted or completed rape in her/his lifetime. In the absence of effective treatment, sexual assault survivors are at increased risk for numerous physical and mental health problems, including depression, post-traumatic stress disorder, and substance abuse.

Objectives:
To compare the efficacy of client-centered therapy (CCT), eye movement desensitization and reprocessing (EMDR), and hypnotherapy in the treatment of sexual assault survivors at the Sexual Assault Center (SAC) in Nashville, TN.

Methods and Materials:
Retrospective review of the records of adult clients of the SAC with a history of rape and/or childhood sexual abuse. Clients were assessed at intake, quarterly, and at exit using the Global Assessment of Functioning (GAF) Scale.

Results:
1. CCT, EMDR, and hypnotherapy are equally efficacious in the treatment of adult survivors of childhood sexual abuse, with average GAF improvements of 6.42+/-.1.35 (n=52), 10.23+/-.3.13 (n=13), and 7.72+/-.1.94 (n=25) for CCT, EMDR, and hypnotherapy, respectively (p=.369 by one-way ANOVA). 2. Hypnotherapy is superior to CCT and EMDR in the treatment of rape survivors, with average GAF improvements of 16.00+/-.3.32 (n=7), 6.93+/-.1.48 (n=41), and 3.17+/-.1.82 (n=6) for hypnotherapy, CCT, and EMDR, respectively (p=.026 by one-way ANOVA; p<.05 for hypnotherapy v. CCT and hypnotherapy v. EMDR by Tukey’s HSD).

Conclusions:
With the exception of hypnotherapy in the treatment of rape survivors, there are no significant differences in efficacy among the therapeutic modalities currently employed by the SAC.

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Mentor(s) and Departments:
Richard Shelton, MD, Department of Psychiatry, Vanderbilt University Medical Center

A SURVEY OF HISPANIC HEALTH BEHAVIORS AND DIABETES KNOWLEDGE

Luis Huerta
Community Health

Objectives:
The main objectives were to develop an increased understanding of the health behaviors of the Hispanic community in Nashville, to increase knowledge of diabetes among Hispanics in Nashville, and ultimately, to decrease the incidence of diabetes among Hispanics in Nashville.

Products Developed:
A literature review was developed which focused on diabetes education.
A survey on diabetes prevention was also produced. A pamphlet with practical tips on diabetes care was created for Hispanics. Finally, a grant proposal was developed for Catholic Charities of Tennessee.

**Brief Description:**
A survey of Hispanic health behaviors and knowledge of diabetes was administered in order to help develop a diabetes prevention curriculum for Hispanics.

**Summary:**
A survey was performed over approximately four weeks at Siloam Family Health Center. The study population was 144 Hispanics, almost all immigrants, who answered questions about their general health practices and their diabetes knowledge. Of those surveyed, 65% understood the causes of diabetes, including poor diet and lack of exercise. At the same time, many people reported poor health habits, including a lack of exercise. Using these results, a diabetes prevention curriculum is being developed for recent Hispanic immigrants that will focus on practical tips.

**Conclusions:**
Overall, the survey results suggest that Hispanics have a good grasp of what they need to do to prevent diabetes but, for some reason, they are not making the necessary changes in their lifestyles. Furthermore, these results imply that diabetes prevention efforts in Hispanics should focus on practical tips for healthy living rather than repeating basic information with which many Hispanics are already familiar.

**Acknowledgements:**
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**Mentor(s) and Departments:**
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**HEALTHCARE ACCESS FOR GRUNDY COUNTY CHILDREN ENROLLED IN TENNCARE**

**Charles Phillips**
*Community Health*

**Objectives:**
The objectives of this study were to determine: 1. Where parents take their children to see primary care providers (PCP’s), specialists, and dentists, in the absence of many healthcare services located within the borders of Grundy County. 2. The parent’s knowledge and utilization of services provided by TennCare, such as transportation assistance to appointments. 3. The number of denials of care by TennCare or healthcare providers.

**Brief Description:**
This study examines access to healthcare and utilization of TennCare by children living in Grundy County, TN, as reported by their parents or guardian.

**Summary:**
Parents with children on TennCare completed an interview questionnaire. Most interviews were completed in-person at the participant’s home; a small number were completed by phone. A total of 60 families participated and information was collected for 130 children.

**Conclusions:**
TennCare provides coverage for over half the children in Grundy County. Most children visit primary care providers (PCP), dentists, and specialists at rates comparable to other areas of the country. However, lack of access to mental healthcare poses a major concern. When TennCare denies coverage for treatment, families overwhelmingly accept this decision without utilizing TennCare’s appeals process. Thirty-eight of 60 families (63%) reported a denial of care for at least one child by a healthcare provider, pharmacy, or TennCare. No family interviewed had ever filed an appeal about any of these denials. Families rely solely on their PCP to correct or circumvent any TennCare denial. This lack of parental response leaves no safety net for children who are severely ill and experience healthcare denials.

**Acknowledgements:**
I would like to thank Barbara Clinton, Barbie Chadwick, the Center for Health Services, and the Tennessee Justice Center for their support.

**Mentor(s) and Departments:**
Dr. Lynn Webb, Vanderbilt University School of Medicine

DEPRESSION IN LOW-INCOME MOTHERS PARTICIPATING IN A HOME VISITATION PROGRAM

**Katherine Shaw**
*Community Health*

**Objectives:**
1. To quantify the prevalence of depression and associated factors 2. To identify barriers to treatment of depression 3. To recommend ways the program can further address depression

**Products Developed:**
1. Report outlining findings and recommendations to improve the MIHOW’s mental health curriculum 2. Brochure about Depression

**Brief Description:**
This project evaluated the prevalence and barriers to treatment of depression in low-income mothers participating in the MIHOW (Maternal Infant Health Outreach Worker) Home Visitation Program.

**Summary:**
Methods: Focus groups were conducted with staff from six MIHOW sites. Additionally, we collected demographic data and administered the Center for Epidemiologic Studies Depression Scale (CES-D) to MIHOW mothers. Results: Focus groups identified cultural barriers as the main factor that prevents depressed mothers from seeking treatment. The following were associated with higher CES-D scores, with a higher score indicating a greater number of depressive symptoms: community setting (rural>urban; \( \chi^2 = 72.10, df = 3, p < 0.0001 \)), marital status (divorced/widowed>partnered>single; \( \chi^2 = 17.99, df = 9, p = 0.035 \)), and employment level (not employed>full time>part time; \( \chi^2 = 31.54, df = 6, p < 0.0001 \)). Income, age, and education level were not significantly associated with CES-D score, although the lowest income group (<$300/month) had significantly higher CES-D scores when compared to higher income mothers (t = 2.267, df = 125, p = 0.025).

**Conclusions:**
Depression is common in the population served by the MIHOW program, and varies by location and specific demographic variables. This project recommends solutions to address both the unique needs of each MIHOW site and the mental health component of the MIHOW training curriculum.

**Acknowledgements:**
Barbie Chadwick, Barbara Clinton, and Diane DeTrizio, Vanderbilt Center for Health Services
RURAL APPALACHIAN KNOWLEDGE AND ATTITUDES CONCERNING HUMAN PAPILLOMAVIRUS AND THE HPV VACCINE

Sarah Tiggelaar
Community Health

Objectives:
To determine knowledge and attitudes concerning cervical cancer, HPV, and the HPV vaccine, and to identify barriers that prevent childhood vaccination in rural Appalachia.

Products Developed:
An HPV vaccine brochure is being developed by the study investigator that will be appropriate for rural Appalachian populations.

Summary:
A public health survey was developed and implemented for subjects in rural Tennessee and Kentucky concerning subject knowledge of Human Papillomavirus (HPV) and the HPV vaccine.

Conclusions:
During the summer, the investigator lived in Jellico, TN and administered a two-page public health survey to adults in three rural family medicine clinics. The chosen clinics represented a range of rurality from extremely isolated to a small college town. Simultaneously, the investigator shadowed doctors in the clinics and the small hospital in Jellico. From observations and interactions with patients, conclusions were that many people in these populations do not have much knowledge of the HPV vaccine, which the survey results confirmed. Only 42% of those surveyed believed the vaccine could prevent cervical cancer and only 8% had vaccinated their children. Lack of information was cited as the most significant barrier to getting the vaccine. Of respondents who agreed that children should receive the HPV vaccine, results showed that they possessed more HPV knowledge, suggesting the importance of education.

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Dr. Lonnie Burnett, Department of Obstetrics and Gynecology

TRAINING UNDERGRADUATES TO MENTOR ADOLESCENTS IN THE TENNESSEE KIDS OVERCOMING PROGRAM

Eric S. Wise
Community Health

Objectives:
1. To design a curriculum to train undergraduates to work with obese adolescents enrolled in the community-based program Tennessee Kids Overcoming (TKO)
2. To evaluate the effectiveness of the curriculum in enhancing the undergraduates’ abilities to work with the adolescents.

Products Developed:
Two literature reviews (one for curriculum development and one for utilizing focus groups), revised powerpoint-based curriculum and comprehensive instructor’s guide, survey analysis from the focus group, and survey analysis from the pilot use of the curriculum.

Summary:
A curriculum was developed to train undergraduate exercise science students at Lipscomb University to work with obese adolescents in the context of the community-based program Tennessee Kids Overcoming (TKO).

Conclusions:
After extensive literature review and discussion with members of the community, a curriculum was designed for training Lipscomb University undergraduates to work for TKO. After the first curriculum was designed, a focus group was held to refine the presentation. The curriculum was ultimately piloted to a class of Exercise Science students who were to act as TKO mentors. Survey assessments were administered before and after the presentation was delivered, as well as at semester’s end, to evaluate the curriculum for effectiveness and future improvements.

Acknowledgements:
Dr. Jay Groves, mentor and Director of the Vanderbilt Dayani Center, Dr. Kent Johnson, Professor of Kinesiology, Lipscomb University, Mr. Eric Seguin, Exercise Physiologist, the Vanderbilt Dayani Center, Ms. Barbara Clinton, Director, Community Health, Ms. Barbie Chadwick, Community Health consultant, fellow community health emphasis students and Ms. Diane DeTrizio and Mr. Andy D’Alessandro, research assistants.

Mentor(s) and Departments:
Dr. Jay Groves, Vanderbilt Dayani Center (primary mentor) and Dr. Kent Johnson, Department of Kinesiology, Lipscomb University (community mentor).
SURVEY OF SATISFACTION LEVELS IN PARENTS OF CHILDREN WITH AN AUTISM SPECTRUM DISORDER (ASD)

Sheri-Ann Wynter
Community Health

Objectives:
1. Describe the experience of parents of children with a diagnosed ASD.
2. Determine the association between parental satisfaction and pediatrician knowledge and behaviors. 3. Compare the experiences of parents who changed pediatricians to those who did not.

Products Developed:

Brief Description:
Parents were recruited to complete a 30 question, anonymous, online survey with questions about family demographics, the child’s diagnostic history, and opinions about their pediatrician.

Summary:
Despite expressing concern at an average age of 2.2 years, parents waited an average of 2.6 years for an ASD diagnosis. Most parents (65%) were likely to refer others to their child’s current pediatrician. Parents were most satisfied with pediatricians’ knowledge of their child’s medical needs and least satisfied with their knowledge about alternative treatments and support groups. Parents were most satisfied with pediatricians’ supportiveness and interactions with their child and least satisfied with their provision of materials. Parents who changed pediatricians (22% changed before the child’s diagnosis, 35% after the diagnosis, and 4% both times) were significantly more satisfied with their current pediatrician’s knowledge of ASD (p=.045) and its diagnosis (p=.013), knowledge about support groups (p=.003) and provision of letters (p=.015), materials (p=.002), and follow-up (p=.035) relative to parents who had not changed.

Conclusions:
Results revealed a long wait time for ASD diagnosis despite parents showing early concerns. Specific aspects of pediatrician behavior and knowledge were associated with parental satisfaction. Providing information about support groups and alternative treatments may improve parent satisfaction. Further studies should investigate the effect of changing pediatricians on the child’s care.

Acknowledgements:
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Mentor(s) and Departments:
Wendy Stone, Ph.D., Department of Psychological Sciences, Vanderbilt University Medical Center.
Global Health

The Global Health focus area provides students with the opportunity to expand their knowledge of health issues of international significance through research projects in developing countries. Potential projects span a broad range of current themes in global health; from medical sciences and clinical investigation to socio-cultural correlates of health and health care delivery. Participation in a Global Health elective and other directed study provides students with the foundation necessary for future work as international clinicians and researchers. The Global Health focus area targets health problems of resource limited settings, including diseases of poverty and the tropics.

“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.”

Sten Vermund, M.D., Ph.D. is Professor of Pediatrics, Amos Christie Chair in Global Health, Director of the Institute for Global Health at Vanderbilt, and the Principal Investigator for the HIV Prevention Trials Network (HPTN), funded by the National Institutes of Health (NIH). Dr. Vermund has been conducting HIV research domestically and internationally for over 20 years and has a related interest in human papillomavirus, STDs, and women’s health. A pediatrician with special interests in adolescent medicine, his research focuses on infectious disease epidemiology and HIV Prevention. Dr. Vermund served as Branch Chief of the Epidemiology Branch, DAIDS/NIAID/NIH from 1988 to 1994. He has founded two overseas non-profit organizations. In 2000, he began the Centre for Infectious Disease Research in Zambia (CIDRZ) with colleagues in Zambia and at the U. of Alabama at Birmingham. CIDRZ is now a $34 million per year research and HIV service enterprise. In 2007, he founded Friends in Global Health, LLC, affiliated with Vanderbilt, to spearhead HIV care and treatment in Mozambique and Nigeria. Nature reported in 2008 that Dr. Vermund ranked third for the number of NIH grants given to any principal investigator in the prior year. He has published over 340 manuscripts and book chapters.
HIV TESTING IN ARGENTINA: IMPROVING ACCESS AND OPTIONS

Christina Ahn
Global Health

Background/Problem:
The 2007 estimates show that approximately 50% people living with HIV/AIDS in Argentina are unaware of their sero status. Since diagnostic HIV testing is the gateway to all free, publicly-funded HIV/AIDS treatment, the policies, procedures and barriers around HIV testing in Argentina warrant examination and discussion.

Objectives:
To examine conventional and rapid HIV screening practices and review currently available testing options in Argentina.

Methods and Materials:
Literature review to assess the use of rapid HIV testing among diverse groups in Argentina, followed by a survey to manufacturers to compile a current list of rapid HIV tests approved for use in Argentina and their performance characteristics.

Results:
There are currently 3 rapid HIV tests approved for use in Argentina that are approximately double the cost of conventional screening tests. The sensitivity and specificity of the tests range from 99.4 to 100 and 99.6 to 100, respectively. With fast results and sensitivity and specificity comparable to conventional ELISA, rapid HIV tests have the potential to significantly impact the delivery of HIV services.

Conclusions:
The utility of rapid testing has already been demonstrated to prevent mother-to-child transmission in women with inadequate prenatal care in Argentina but research is needed to explore the feasibility of rapid HIV testing among diverse populations in various clinical and nonclinical settings. The fact remains that the cost is a significant barrier to widespread implementation.

Acknowledgements:
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Mentor(s) and Department:
Dan Masys, M.D., Department of Biomedical Informatics, Vanderbilt University School of Medicine

IMPACT OF HOME BASED CARE ON HIV OUTCOMES IN RURAL ZAMBIA

Christopher Estopinal
Global Health

Background/Problem:
Antiretroviral therapy (ART) is becoming increasingly available in rural resource-poor settings. These areas often lack infrastructure and human resources necessary to run HIV clinics using traditional first-world models. The “home-based care (HBC)” model, in which community volunteers care for and counsel neighbors, has achieved success in tuberculosis initiatives. This model is now being used by HIV clinics, rural and urban alike, and its impact on patient outcomes must be assessed.

Objectives:
To evaluate the HBC program at Macha Mission Hospital (MMH), a hospital caring for approximately 3,000 HIV-positive patients in rural Zambia.

Methods and Materials:
Records of 519 patients were included. Each patient’s gender, residence, days on treatment, and adherence were recorded along with age, body mass index (BMI), CD4 count, and hemoglobin concentration (Hgb) at treatment initiation. Patients were labeled “HBC+” if living within the catchment area of an HBC group and “HBC-” if not. Patients were classified as positive treatment outcomes (alive and receiving ART) or negative treatment outcomes (dead, stopped treatment, lost to follow-up). Multivariate analysis was performed to assess association between “HBC+” classification and positive treatment outcomes.

Methods and Materials:
We conducted a retrospective cohort study of infants (0-24 months) tested from Nov 2007- Nov 2008 in the EID program. Study variables included patient demographics and exposure to prevention interventions. Rates of follow up of mother-infant pairs and HIV test results in infants were the main outcome measures.

Results:
The number of infants referred to the ART clinic nearly doubled after the initiation of EID, compared to the previous year. One hundred eighty-three infants were brought for EID; the rate of follow-up of mother-infant pairs from antenatal care to EID was only 19%. HIV prevalence in the 169 infants tested with the DBS-PCR test was 18%. Maternal HAART was a statistically significant predictor of follow-up from antenatal care to EID and negative HIV test in the infant.

Conclusions:
The application of the DBS PCR test can lead to earlier diagnosis and treatment of HIV-infected infants, and facilitate quality improvement of prevention programs. However, the impact of this diagnostic technology, particularly in rural health facilities, is limited by infrastructure, human resources, and the need to address the socio-cultural dimensions of HIV infection in women and children.

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Mentor(s) and Department:
Alfredo Vergara, Ph.D., Institute for Global Health, Vanderbilt University School of Medicine
Results:
Preliminary analysis gave no association between “HBC+” classification and positive treatment outcomes. Higher BMI, CD4, and Hgb at treatment initiation were associated with positive treatment outcomes.

Conclusions:
Predictors of patient outcomes (BMI, CD4, Hgb) were coherent with the literature. While the data suggested no significant impact of HBC on HIV outcomes, further investigation is crucial in better understanding the relationship between HBC and patient morbidity/mortality in this rural Zambian setting.

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Mentor(s) and Department:
Sten Vermund, M.D., Ph.D., Institute for Global Health, Vanderbilt University School of Medicine

EVALUATING INFORMED CONSENT IN GLOBAL ENTERICS MULTICENTER STUDY (GEMS)

Saira Khan
Global Health

Background/Problem:
GEMS investigates diarrheal disease in children under 5 years of age in developing countries, to develop vaccines against enteric disease. The consent form, written in Urdu, outlines the project’s purpose, risks/benefits, and choice to participate.

Objectives:
To explore which factors contributed positively or negatively to participant understanding of the purpose of GEMS.

Methods and Materials:
A checklist for interviewers, based on consent protocol, and a brief questionnaire to assess participant understanding were created. Thirty-eight interviews of caregivers of cases and controls were conducted at GEMS sites in Karachi, Pakistan

Results:
The mother tongues of 97% of participants differed from the language of the consent form. A majority of participants lacked formal schooling and only 23.5% were literate. Overall, 46% of participants understood GEMS purpose as determining etiologies and/or developing vaccines against diarrheal disease. Twenty-nine percent thought the survey was part of their child’s healthcare; the majority of these were mothers of cases. Instances in which the interviewer encouraged participants to ask questions, and asked questions of participants, fared better in comprehension (62% and 53%, respectively), compared to situations in which no encouragement was offered or no confirmatory questions asked (9% and 29%, respectively). Eighty-nine percent of participants felt obtaining consent is important; 11% were unsure.

Conclusions:
Working with diverse and under-educated populations places the onus upon interviewers to engage participants in dialogue to confirm understanding. Indeed, engaged interaction increases participant comprehension. Care must be taken to ensure participants are able to distinguish research from the healthcare of their children. Participants value the consent process, and are willing to spend time on it.

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FAITH-BASED HIV/AIDS PREVENTION AND CARE IN SOUTHERN SUDAN

J. Matthew Kynes
Global Health

Background/Problem:
Conflict in southern Sudan has hindered development, creating an area vulnerable to the spread of HIV/AIDS. Elsewhere in Africa, local religious organizations have played key roles in providing prevention and care activities. Christian churches are prominent in southern Sudan and could serve to help curb the spread of HIV/AIDS there.

Objectives:
To examine the opinions of church leaders in Nimule, Sudan about HIV/AIDS prevention and assess the prevention and care activities their churches provide.

Methods and Materials:
There are 11 churches within Nimule. A 22-question tool was developed and distributed to leaders of these churches to survey attitudes about HIV/AIDS prevention and assess related programming. Eighteen pastors and elders from 10 churches responded. The quantitative and qualitative results of the survey were analyzed.

Results:
All respondents were aware of HIV/AIDS in the community, and 50% agreed that condoms were effective in preventing HIV/AIDS. Prevention efforts were more common than care provision. There was only one on-going prevention program, although 6 congregations had received an HIV/AIDS presentation and 67% of leaders mentioned HIV/AIDS in messages sometimes or often. Four churches had provided HIV-specific care, although only one church noted material care provision and no programs were on-going. Barriers cited included lack of funding, organization, pastoral training, and stigma.

Conclusions:
The religious community in Nimule is accessible, but underutilized in HIV/AIDS activities. Although HIV/AIDS is discussed, coordinated prevention and care efforts are lacking and barriers to mobilization remain.

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Mentor(s) and Department:
Sten Vermund, M.D., Ph.D., Institute for Global Health, Vanderbilt University School of Medicine
USING MORBIDITY CALENDARS TO ASSESS CLINICALLY RELEVANT ILLNESSES IN WESTERN GUATEMALAN WOMEN

Robert B. Lindell  
Global Health

Background/Problem:  
In 2002, Primeros Pasos opened as a clinic serving children in the Palajunoj Valley. In 2006, the clinic began accepting adult patients and has seen tremendous growth in adult consultations. No other clinics provide health services to this population.

Objectives:  
To assess clinically relevant illnesses in women in the Palajunoj Valley using two-week morbidity calendars.

Methods and Materials:  
Women 18-35 years old without current symptoms were eligible for inclusion. Participants were questioned regarding their experience of 20 common symptoms during the previous 14 days. For each positive symptom, the date of onset, duration, severity, source of treatment, and barriers to care were recorded. Constellations of concomitant symptoms were defined as illnesses, and illnesses treated in a clinic or self-reported as severe were defined as clinically relevant illnesses (CRIs).

Results:  
Of 84 women surveyed, 32% experienced a CRI in the previous 14 days. The most common symptoms were sore throat, stomach pain, and cough. Compared to patients with non-serious symptoms, patients with CRIs were more likely to seek clinical care. Patients with fever or GI symptoms were significantly more likely to seek clinical care than patients with respiratory symptoms. Twenty-eight percent of patients with CRIs received no care from any source. Barriers to care were reported by 33% of patients and included cost, transportation, and child care.

Conclusions:  
The prevalence of illness in this community remains high despite access to clinical services. Understanding the barriers to care and the underlying prevalence of CRIs will allow medical providers to better care for the health of this underserved population.

Acknowledgements:  
Kalya Vardi, Brent Savoie, Jessica González

Mentor(s) and Department:  
Sten Vermund, M.D., Ph.D., Institute for Global Health, Vanderbilt University School of Medicine

UNDERSTANDING THE UNDERLYING PROTECTIVE EFFECT OF BREAST MILK IN PRETERM INFANTS

Yamini Rao  
Global Health

Background/Problem:  
The protective role of breastfeeding against severe lung disease is well-documented, but the mechanism is unknown. A differential gender response to respiratory infections and to the protective effect of breast milk in preterm infants was recently determined showing that non-breastfed girls are most susceptible to severe lung disease, challenging the theory of protection from passive transfer of humoral immunity which would be gender indifferent.

Objectives:  
The objective of this study was to determine what non-specific modulatory factors could play a role in the differential gender response of preterm infants to breast milk protection. The factors tested were varying estrogen levels at human breast milk concentrations and gender specific differences and the effect of breast feeding in Th polarization

Methods and Materials:  
Preterm infants at Hospital Sarda in Buenos Aires were enrolled, and blood samples were taken at 40 weeks, 3 months, and 6 months of life. Isolated PMNCs were stimulated with estradiol within the normal breast milk concentrations (10pg/ml to 1x106pg/ml E2). This was followed by Elisa proliferation assay and flow cytometry, and Hu-IFN-gamma and Hu-IL-4 levels were measured in the supernatant to determine Th1 versus Th2 bias.

Conclusions:  
T cell response to estradiol between boys and girls (n=4) and breast fed infants versus formula fed infants (n=6) showed no statistically significant results. There was a slight Th2 bias (n=18) in breastfeeding females as compared to breastfeeding males. This value was not statistically significant, but proves a need for future research into non-specific modulation of immune response between genders and milk feeding patterns in premature infants.

Mentor(s) and Department:  
Fernando Polack, M.D., John Williams, M.D., Division of Pediatric Infectious Diseases, Monroe Carell, Jr. Children’s Hospital at Vanderbilt

GLOBAL HEALTH

GENTAMICIN PMMA ANTIBIOTIC BEADS IN SURGICAL TREATMENT OF POST-TRAUMATIC OSTEOMYELITIS

Nedim Ruhotina  
Global Health

Background/Problem:  
Sarajevo, capital of Bosnia and Herzegovina, was the epicenter of the Bosnian Civil War from 1992 to 1995. The city was under siege for 43 months with nearly 15,000 killed and 40,000 wounded. The University of Sarajevo Orthopaedics Department treated the majority of patients with blast injuries to the extremities. Many of these patients developed post-traumatic osteomyelitis, or bone infections, of the long bones.

Objectives:  
To determine the effectiveness of surgically implanted Gentamicin Polymethylmethacrylate antibiotic beads vs. surgical debridement and parenteral antibiotics in managing post-traumatic osteomyelitis due to Grade III fractures.

Methods and Materials:  
This retrospective chart review study was conducted at the University of Sarajevo Orthopaedics Department. Patients were included if they sustained grade III open fractures of the tibia and femur and were seen within 24 hours of injury. Charts were screened for variables such as medical history, microorganisms isolated, location of fracture; type of fixation, flap coverage and type of antibiotic treatment administered. Outcome measures were based on resolution of infection and union of fracture.

Results:  
Control group: treated with parenteral antibiotics and surgical debridement. Total of 40 patients were included with an average 4.5 year follow-up.
Outcomes: 27% resolution of infection, 77% union of fracture. Experimental group: treated with antibiotic beads, parenteral antibiotics, and surgical debridement. Total of 30 patients were included with an average 10.8 year follow-up. Outcomes: 70% resolution of infection, 85% union of fracture.

Conclusions:
Gentamicin-PMMA beads are effective in delivering high concentration of antibiotic and managing surgical dead space in infected Grade III fractures with significant soft tissue compromise.

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ASSESSING MOBILE ROUTINE, OPT-OUT HIV TESTING AND COUNSELING IN RURAL SOUTHERN ZAMBIA

David Silvestri
Global Health

Background/Problem:
HIV testing and counseling is important for early ART access and reduced HIV transmission. However, in Sub-Saharan Africa, it is estimated that 90% of adults have never been tested and 80% of HIV-infected adults do not know their HIV status. Routine, opt-out HIV testing has improved HIV detection in several Sub-Saharan African nations (notably Botswana) and is currently recommended by the World Health Organization. However, in Zambia, where HIV prevalence exceeds 15%, testing and counseling remains voluntary and opt-in.

Objectives:
Researchers sought to compare HIV rates detected under standard opt-in and routine opt-out testing systems.

Methods and Materials:
HIV testing and counseling was performed at a mobile medical clinic at four sites in rural Southern Province, Zambia. Medical care providers were divided into two groups—one referring patients for HIV testing only upon patient request or demonstration of signs and symptoms of HIV infection (voluntary, opt-in) and the other referring all patients ages 15-49 for HIV testing (routine, opt-out). HIV prevalence was assessed by patient age, sex, and type of referral.

Results:
1189 adults (ages 15-49) were tested for HIV-1/2 infection. Males were more likely to test positive than females (13.3% vs. 11.1%). Standard, opt-in VCT was not associated with a significantly higher overall HIV detection rate than the routine, opt-out PITC approach (11.7% vs. 11.8%; p=0.98). 96.3% of adult respondents were in favor of PITC, with males more likely to be in favor than females (p<0.01).

Conclusions:
Routine, opt-out HIV testing and counseling in mobile clinics offers an important means for early HIV diagnosis in remote HIV-endemic regions lacking reliable access to testing facilities.

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Mentor(s) and Department:
Jeffry McKinzie, M.D., Department of Emergency Medicine, Vanderbilt University Medical Center

NEEDS AND PROBLEMS OF THE ELDERLY AND THEIR CAREGIVERS IN RURAL VELLORE, SOUTH INDIA

Merina Thomas
Global Health

Background/Problem:
The majority of India’s elderly reside in rural areas and they are often neglected by their caregivers. The social support provided for the elderly population in the Sathumadurai village of Vellore, South India has not been studied previously.

Objectives:
1. To identify needs and problems of the elderly regarding social support.
2. To identify needs and problems of caregivers regarding relationships with the elderly.
3. To determine what suggestions the elderly and caregivers have for improving quality of life in a rural setting.

Methods and Materials:
This qualitative and cross-sectional study was conducted in Vellore, South India. Focus group discussions were conducted for groups of female caregivers, male caregivers, and female elderly. A questionnaire was administered to the elderly population to provide a larger perspective regarding elderly social support.

Results:
A total of 162 questionnaires were returned by people 60-years-old and older in the Sathumadurai village with 0% missing information. When adjusting for other predictors, on average social support decreased by 2.73 points when age increases from 62 to 72, increased by 3.47 points when SES increases from 2 to 8.8. Social support was 2.78 points less for individuals with no income when compared to those with income.

Conclusions:
Rural elderly who were older, had a lower SES, or had no income had decreased social support by caregivers. Collecting information regarding the needs of the elderly and their caregivers is vital to determining the services provided to these groups. An elderly daycare in the village will be implemented as a result of this study.

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Mentor(s) and Department:
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PREVALENCE OF DIABETIC NEUROPATHY IN A NIGERIAN GENERAL MEDICAL CLINIC

Chinenye Usoh
Global Health

Background/Problem:
Diabetic neuropathy (DN) is a consequence of inappropriately managed diabetes. In developing countries, such as Nigeria, there have not been many studies done on the prevalence of DN. And the studies that have been done, exhibit wide variability in results (from 5%-75%).

Objectives:
The aim of this research was to determine the prevalence of DN in a Nigerian private hospital. Variables that were examined include gender, age, body mass index, and occupation. Research questions were: 1. Is there a difference in DN prevalence between men and women? 2. Does occupation influence susceptibility to DN? 3. Does BMI and age correlate with prevalence and intensity of DN in the BMC General Medical Clinic?

Methods and Materials:
The research was done at Baptist Medical Centre in Ogbomoso, Nigeria. To determine presence and level of diabetic neuropathy, we used the Michigan Diabetic Neuropathy Score (MDNS) and Michigan Neuropathy Screening Instrument (MNSI). These previously validated surveys contained a questionnaire about the participant’s level of sensation and also tests of reflexes, muscle strength, and sensory impairment.

Results:
Seventy-two percent of participants had DN. Females and males had an average MDNS of 11 and 9.5 respectively (p=0.12). Diabetic civil workers had the lowest average MDNS (7.0), while educated professionals (11.0) and labor workers (11.0) had the highest (p=0.233).

Conclusions:
Further study of these trends is needed. Civil workers may have the lowest MDNS because the Nigerian political system gives more power to those that work for the government, and therefore better access to healthcare.

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Mentor(s) and Department:
Margaret Tarpley, M.L.S., Department of Surgery, Vanderbilt University Medical Center

EVALUATION OF HEALTH COMPLAINTS AMONG INDIGENOUS ADULTS BASED ON DEMAND FOR CLINIC SERVICES

Kalya Vardi
Global Health

Background/Problem:
Primeros Pasos (PP), a clinic located in the western highlands of Guatemala, has provided walk-in care to indigenous adults since late 2005. Given the paucity of data on the health needs of this population, the services and medications which PP offers have largely been dictated by demand. The researchers and PP staff agreed that quantifying what complaints brought adults to the clinic would be an important first step towards understanding the health needs of this population, evaluating the services and care offered by the clinic, and improving those services and the overall health of the population.

Objectives:
The principal objective of this study was to help PP determine where to focus its limited resources for adult care by quantifying what complaints brought adults to the clinic.

Methods and Materials:
Researchers conducted a retrospective chart review for all adult walk-in visits from January 2005 through April 2008, excluding prenatal care. The data extracted from the charts included: age, gender, month of visit, year of visit, community name, chief complaint, chief complaint duration and other complaints.

Results:
The review included 975 visits. The most common presenting complaints were gastrointestinal (32.5% of visits), upper respiratory (23.3%), headache (19.7%), itching (16.1%) and pain in another specific location (14.0%). The category “gastrointestinal” clusters stomach pain, nausea or vomiting, and diarrhea. “Upper respiratory” clusters sore throat and cough.

Conclusions:
The data have implications for resource allocation, including staff training, staff recruitment, equipment purchases and community programming. In particular, the data will be useful for defining research priorities.

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Mentor(s) and Department:
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A HEALTHCARE RESOURCES ASSESSMENT NEAR QUITO, ECUADOR: EVALUATING COMMUNITY PERCEPTIONS

Carmen Wolfe
Global Health

Background/Problem:
In August 2007, Manna Project International (MPI), a Vanderbilt-affiliated non-governmental organization, established a new project site in a rural community outside of Quito, Ecuador. MPI works within communities to strengthen economic development resources, provide educational supplementation, and facilitate increased delivery of health services.

Objectives:
In an effort to improve clinical services in their catchment area, MPI sought to evaluate the availability of prenatal care and maternal/fetal healthcare, and to determine best way to serve these needs.

Methods and Materials:
A series of door-to-door interviews with community members was carried out to collect quantitative and qualitative data for a health resources assessment.
Results:
Eighty-six percent of women reported that they received prenatal care, and all women had access to skilled delivery. Positive attitudes towards these health factors are important health strengths of the community. Specific health needs were identified in unexpected areas. Sixty-six percent of respondents did not regularly seek preventative medical care for themselves or their children. While all respondents felt that they had access to basic medical services, just over half reported dissatisfaction with the resources available, travel time to healthcare facilities, costs associated with private clinics, and waiting times at public clinics. Health literacy proved to be another major issue, as many respondents were unsure about disease prevention methods, facts about prevalent illnesses, and the importance of preventative medicine.

Conclusions:
Leveraging the observed healthcare strengths and specifically addressing healthcare weaknesses, MPI will use these baseline health data to provide appropriate clinically-based services, design health care education programs, and measure future health improvements.

Mentor(s) and Department:
Elizabeth Heitman, Ph.D., Department of Medicine and Department of Anesthesiology, Vanderbilt University Medical Center

CANCER IN THE SETTING OF HIV IN LIMA, PERU

Irving Ye
Global Health

Background/Problem:
HIV/AIDS remains a burden on many patients around the world. While new advances reduced some AIDS-defining opportunistic diseases and cancers, non-AIDS-defining cancers have increased with the use of anti-retroviral therapy (ART). The project seeks to track cancer cases among HIV/AIDS patients in Peru, as part of the Caribbean, Central and South America network for HIV epidemiology studies (CCASAnet).

Objectives:
To determine the prevalence of cancers in HIV-infected patients treated at Instituto de Medicina Tropical Alexander von Humbolt (IMT-AvH), Universidad Peruana Cayetano Heredia, Lima, Peru between 1990 and 2002.

Methods and Materials:
The study was conducted on-site at IMT-AvH using hospitalization records and patient history files from the clinic’s Special Archives. Specifically, the patient files used for study were the Hospital Discharge Records, which listed the final diagnoses of each patient at time of discharge. Each patient discharge file from 1994-2001 was screened for HIV and cancer status. For cases of positive HIV plus cancer diagnoses, the complete patient history was obtained from the Special Archives and reviewed for descriptive data.

Results:
Between 1994 and 2001, there were 4909 hospitalizations of unique patients at IMT-AvH, with 878 (17.9%) HIV-positive patients. The average cancer prevalence in HIV patients was 4.2% over the time period, with no statistically significant changes in cancer rate and composition of cancer types (Kaposi sarcoma and unspecified lymphoma).

Conclusions:
From preliminary data for cancer cases in HIV-positive patients hospitalized at IMT-AvH, there were no statistically significant results that showed changes in cancer prevalence or composition in HIV-patients.

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The student experience in the area of Healthcare and Public Health Research and Management is designed around two tracks: 1) Health research and 2) Health management. The research track is focused on hypothesis-driven investigation in a field of healthcare research, which includes clinical epidemiology and outcomes research, clinical economics and management science, clinical improvement and operations research, chronic disease and molecular epidemiology, health behavior and education, and health policy. The healthcare management track is focused on a healthcare management science internship that includes a quality improvement project. It is expected that the student will become a successful member of an active research program or clinical management team and will have a clearly defined project to be completed in the time allotted. “In the Healthcare and Public Health Research and Management Emphasis area, I was impressed with the students’ abilities to articulate an important question, identify an appropriate study design, implement the study with careful measurement and analyze and interpret the findings. The portfolio of projects represented the broad range of topics characterized by this area. I enjoyed the students’ passion and dedication in their work. From prevention, diagnosis, treatment, and prognosis, to the organization and management of health services and the health policies affecting care delivery, students made meaningful contributions that will improve the quality of health care and I was proud of their accomplishments."

“The research track is focused on hypothesis-driven investigation in a field of healthcare research.”

Robert S. Dittus, M.D., M.P.H. is the Albert and Bernard Werthan Professor of Medicine and Public Health. He is also the Director of the Institute for Medicine and Public Health; Center for Health Services Research; Geriatric Research, Education and Clinical Center; Institute for Community Health, Center for Improving Patient Safety and Quality Scholars Program. He has advanced the methodology of medical decision making, conducted numerous studies delineating the cost-effectiveness of alternative strategies for clinical care, and created multiple clinical research training programs. He is a Senior Quality Scholar of the Department of Veterans Affairs and the founding President of the Academy for Healthcare Improvement.
**SYSTEMATIC REVIEW: MRI AND CONVERSION FROM MILD COGNITIVE IMPAIRMENT TO ALZHEIMER’S DISEASE**

**Katie Atnip**  
*Healthcare and Public Health Research and Management*

**Background/Problem:**  
Mild cognitive impairment (MCI) is the clinical condition of patients who are mildly cognitively-impaired but do not meet criteria for dementia. MCI patients convert to Alzheimer’s disease (AD) at a rate of 10-15% per year, as compared to 1-2% of the healthy elderly population. Researchers have tested markers such as functional and structural imaging, apoE, and CSF-tau to attempt to predict which MCI patients will progress to AD. The ability to establish which patients are at increased risk for AD will allow researchers and clinicians to target interventions to patients who will demonstrate the greatest benefit.

**Objectives:**  
To systematically analyze investigations that address the question of whether MRI can aid in determining risk of conversion to AD for patients with MCI.

**Methods and Materials:**  
This systematic review selected papers from Medline, PsycInfo, and bibliographies from January 1970 to October 2008. Of 2000+ papers, 16 met the inclusion criteria of a prospective study of structural MRI comparison with MCI conversion status after at least one year.

**Results:**  
The papers included 873 MCI patients of whom 369 (42.3%) converted to AD. Region-of-interest (ROI) showed significant prediction of risk of conversion to AD, especially in hippocampal, entorhinal cortex, and ventricular regions. Voxel-based morphometry (VBM) revealed significant atrophy in areas surrounding the hippocampus, inferior frontal gyrus, and superior temporal gyrus.

**Conclusions:**  
ROI and VBM studies revealed that hippocampal atrophy was significantly associated with conversion to AD. Other areas were implicated as well, but more research is required before any specific measurements can be used for prediction of conversion.

**Mentor(s) and Department:**  
Harry Gwirtsman, M.D., Department of Psychiatry, Veterans Affairs Hospital Medical Center, Nashville, Tennessee and Melissa McPheeters, Ph.D., M.P.H., Department of Obstetrics and Gynecology, Vanderbilt University Medical Center

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**FACTORS THAT INFLUENCE PARENT ATTITUDES TOWARD TYPE 1 DIABETES CLINICAL RESEARCH**

**Daniela Buscariollo**  
*Healthcare and Public Health Research and Management*

**Background/Problem:**  
The Type 1 Diabetes (T1D) TrialNET has dramatically increased available clinical trials (T1DCTs) to prevent or reverse T1D. However, these trials may be limited by insufficient patient enrollment for rapid, well-powered study completion.

**Objectives:**  
To identify factors that influence parental willingness to enroll their children in T1DCTs.

**Methods and Materials:**  
Expert opinion, parent focus groups and a pilot test were used to create a survey to probe attitudes toward T1DCTs. The survey consisted of 48 questions including open-ended, yes/no, and Likert scale response formats. Surveys were distributed at Diabetes Family Day (n=21) and the Eskind Pediatric Diabetes Clinic (n=67) at Vanderbilt University Medical Center.
Results:
Response rate was 57% and respondents were predominantly Caucasian (95%) and female (79%). Seventy-five percent of respondents reported awareness of T1DCTs at Vanderbilt. Nearly 50% described themselves as willing to enroll. Willingness to enroll was positively influenced by whether participants had been provided easy-to-understand information about T1DCTs (r=0.55, p<0.01). Self-reported income and concern about diabetes complications positively correlated with willingness. Only 20% recalled being asked to enroll a child by a healthcare provider. Less than 30% of parents reported being comfortable with T1DCT protocols using IV medications, vaccines, or placebo. Parents reporting themselves as more willing to enroll in T1DCTs were more likely to accept these trials (r=0.26-0.49, p<0.01).

Conclusions:
Parents report willingness to enroll their children in T1DCTs. However, only a minority accept methods in current trials. Healthcare providers can encourage parent willingness. Thus, efforts to increase awareness of T1DCTs and their methods may accelerate testing of new therapies for T1D.

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RELATIONSHIP BETWEEN RISING RATES OF CESAREAN SECTIONS AND GESTATIONAL DIABETES

Karen Chen
Healthcare and Public Health Research and Management

Background/Problem:
Cesarean sections are associated with significant maternal and fetal morbidity and represented 31.1% of all live US births in 2006. Gestational diabetes (GDM) has also been rising for the past 10 years and increases the risk of poor delivery outcomes. It is unknown to what degree rising rates of GDM may contribute to rising cesarean section rates.

Objectives:
To determine whether and how the rate of cesarean sections in women with GDM increased from 2002 to 2006.

Methods and Materials:
We used the Nationwide Inpatient Sample (NIS) to identify all women ages 15-50 who had a singleton delivery from 2002 to 2006 and had no previous c-section.

Results:
From 2002 to 2006, the proportion of singleton births delivered by cesarean section increased by 17.6% to 20.4%. The rate of cesarean sections increased by 17.2% among privately insured women with GDM, but only by 12.2% among publicly insured women with GDM. Relative to other types of hospitals, urban teaching hospitals had the greatest increase in the rate of cesarean deliveries of 18.2%. The length of stay for women with gestational diabetes who had a cesarean section did not change significantly.

Conclusions:
We observed significant increases in rates of cesarean sections among women with GDM who were privately insured or delivering in urban teaching hospitals. This disproportionate rise occurs despite no significant change in length of stay, age, or geographic distribution in the US among public-pay and private-pay women.

Mentor(s) and Department:
Melissa McPheeters, Ph.D., M.P.H. and Theresa Scott, M.S., Vanderbilt University Medical Center

ASSESSING PUBLIC HEALTH “ON THE REZ:” APPLYING THE NPHPSP’S LOCAL TOOL TO THE NAVAJO NATION

Aaron Jay Dawes
Healthcare and Public Health Research and Management

Background/Problem:
Assessing the functional capacity of a public health system is a complex and often subjective task. The Centers for Disease Control and the National Association of County and City Health Officials have collaborated to produce guidelines to aid local public health departments in defining and evaluating their function. The National Public Health Performance Standards Program (NPHPSP) comprises three separate assessment instruments, and is the newest product of this ongoing collaboration. The Navajo Nation is the largest reservation in the United States, both in terms of population and landmass. Although proven in other environments, no NPHPSP instrument has ever been applied to the Navajo reservation or to any other Native American population.

Objectives:
To determine the feasibility and usefulness of applying the NPHPSP’s Local Tool to a reservation community.

Methods and Materials:
This study was conducted as a qualitative evaluation of the instrument. Using the Local Tool as a guide, a simplified metric was created to match the knowledge and time constraints of the involved parties. Public health directors from three of the six service units currently administered by the Indian Health Service (IHS) were interviewed. Discussion focused around each service unit’s contribution to the “10 Essential Services” of a public health department, as defined by the instrument.

Conclusions:
While cumbersome, the Local Tool can be efficiently applied in a reservation setting. Due to complex relationship between contributing parties—not the least of which between the IHS and the Navajo Division of Health—the value of the tool requires further scrutiny.

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MAXIMIZING INTERPRETABLE HEART SOUNDS IN THE ED USING DIGITAL AUSCULTATION AND COMPUTERIZED ANALYSIS

Brett Donegan
Healthcare and Public Health Research and Management

Background/Problem:
High noise/signal ratio (NSR) has limited use of stethoscope-based digital phonocardiography in detection of added heart tones (S3, S4) in the Emergency Department (ED) environment. Accurate computer recordings would aid cardiac diagnosis.

Objectives:
Determine the optimal combination of patient position, auscultation location, and stethoscope type capable of minimizing NSR.

Methods and Materials:
Researchers tested two patient positions (semi-supine vs. left lateral decubitus), two auscultation locations (pulmonic vs. mitral), and two digital stethoscopes (ThinkLabs ds32a vs. WelchAllyn Meditron, both recorded to computer) in a tertiary care ED during 2007-2008. Four trained operators performed eight recordings on 88 healthy volunteers. To account for similarities within patients and operators, a linear mixed model was fit to determine what combination of parameters minimized NSR. Correlation and agreement between raters was assessed using Spearman’s rho and Bland-Altman plot. Multivariable mixed modeling was used to assess the influence of operator and subject-specific characteristics.

Results:
Subjects had a median age of 24 years (IQR 23-34) and 37 (42%) were male. NSR decreased with the semi-supine position (absolute change -1.93, p=0.012), ds32a stethoscope (-3.43, p<0.0001), and mitral location (-4.98, p<0.0001). Correlation (Spearman’s rho=0.86) between raters was high. A Bland-Altman plot indicated good agreement between raters’ average NSRs per subject with 94% of measurements within agreement limits. Operator was strongly associated with average NSR; ED room, BMI, sex, and age were not.

Conclusions:
Auscultating with the ds32a stethoscope in the mitral location with the subject semi-supine produced the best (lowest NSR) recordings.

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REHABILITATION AND MILD TRAUMATIC BRAIN INJURY-IS OUTREACH THE PROBLEM?

John Eicken
Healthcare and Public Health Research and Management

Background/Problem:
Patients sustaining traumatic brain injury (TBI) may have negative long term cognitive effects. Intensive post-injury rehabilitation has been shown to improve outcomes in individuals who have suffered TBI.

Objectives:
To determine the barriers associated with access to post-injury cognitive rehabilitation in mild TBI.

Methods and Materials:
A retrospective cohort pilot study of 234 mild TBI patients who sustained their injury between July 2005 and 2007 and were treated at a Level I trauma center were evaluated by phone survey utilizing the Glasgow Outcome Score (GOS) at least 6 months post-discharge. The cohort was blunt trauma patients with a GCS 13-15 and concussion, negative head CT findings, a working phone, in a major metropolitan area or contiguous county ensuring access to adequate rehabilitation services. Patients without post-injury cognitive rehabilitation were asked follow-up questions concerning access. Patients received TBI literature prior to discharge and were contacted by the Tennessee TBI foundation, per state regulation. Chi-square statistical analysis as indicated.

Results:
Of 366 eligible patients, 228 completed the phone survey. Two hundred eleven patients did not receive rehabilitation with 28% believing post-injury rehabilitation was necessary. Twenty-four percent did not recover to the quality of life prior to injury (GOS<5) while 141/228 (62%) were unaware of post-injury rehabilitation services. Fifty-seven (28%) patients who did not receive cognitive rehabilitation subjectively reported they felt it was warranted. There was no association to lower GOS and subjective need. An association between GOS and insurance status (p=.01) was identified.

Conclusions:
This research suggests that the current method of educating patients about mild TBI may not be effective. A lack of knowledge of post-injury cognitive rehabilitation services as well as patient insurance status may play a role for those who could benefit from intervention. Further investigation should be conducted on the current outreach practices at the local and state level to determine why such a large portion of the target population is not aware of the rehabilitation services available.

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DEVELOPMENT OF A MEDICAL STUDENT-RUN, COMMUNITY-BASED OUTREACH: IMPACTS ON STUDENTS AND COMMUNITY

J. Bradford Hill
Healthcare and Public Health Research and Management

Background/Problem:
Community-based efforts bring patients and providers together in more accessible and robust settings, allowing for unique contacts as compared a traditional clinical setting. These outreaches provide opportunities for medical students to derive meaningful, real-world experiences and skills while providing communities with beneficial services.

Objectives:
We had three objectives: 1. Develop a community-based, student-run, monthly blood pressure assessment program; 2. Review its effectiveness and influences on both volunteers and participants; and 3. Pilot the test instruments.
Methods and Materials:
A series of monthly health fairs were held at a local community center. All students received monthly blood pressure measurement instruction and education regarding interview counseling skills. Community members received blood pressure screens followed by an individual educational session with a medical student. Both students and participants were asked to complete questionnaires following their involvement.

Results:
Over 100 community members utilized the services of the health fair over 4 monthly sessions. A total of 14 medical students from Vanderbilt and Meharry medical schools volunteered, with a core group of 5 students who attended nearly every session. Surveys designed to measure both short and long-term impacts and perceptions were administered at the final session with a total of 7 questionnaires completed by participants and 4 completed by students. Students and community members reported positive impacts within both long and short-term domains.

Conclusions:
Medical schools may consider this model and evaluation tool for assessment of both community outcomes and the satisfaction derived from medical student involvement in community health roles.

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ADDRESSING LITERACY AND NUMERACY TO PREVENT EARLY CHILDHOOD OBESITY

Disha Kumar
Healthcare and Public Health Research and Management

Background/Problem:
Over 90 million Americans have poor literacy or numeracy skills. Low health literacy is associated with poorer parental understanding of breastfeeding guidelines, mixing of infant formula, food labels and portion sizes, and higher BMI. Over 26% of preschool children are overweight or obese, and rates are higher among families with lower socioeconomic status. Pediatricians can play an active role in educating families about healthy lifestyle habits.

Objectives:
The aim of this study is to address literacy and numeracy via improved healthcare provider communication and a low-literacy-oriented intervention to promote healthy lifestyles and prevent overweight development.

Methods and Materials:
The STOPLIGHT Toolkit was developed with input from experts in pediatric obesity, nutrition, health literacy and numeracy, cultural competency, and health behavior, and families via cognitive interviewing. A Clear Health Communication Curriculum was created for training pediatric residents to use the toolkit with families. The toolkit can be used as part of anticipatory guidance for each well-child visit from 4 months to 24 months of age. Core topics covered include: breast and formula feeding, portion sizes, reducing juice intake, starting solid foods, limiting television, and promoting physical activity. Each topic encourages shared goal-setting on specific health behaviors.

Results:
One hundred English and Spanish-speaking families with children 6-18 months of age were being enrolled in a 6-month before-after pilot trial.

Conclusions:
A subsequent multicenter randomized control trial will include 1000 English and Spanish-speaking families with children of 4 months followed until 24 months of age. The goal of the intervention will be to promote healthy lifestyles and prevent overweight development.

References:
Available upon request

Acknowledgements:
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Mentor(s) and Department:
Russell Rothman, M.D., M.P.P., Center for Health Services Research, Vanderbilt University Medical Center

VENTILATOR-ASSOCIATED PNEUMONIA FOLLOWING INJURY: PREDISPOSITION TO RECURRENTENCE IN 728 TRAUMA PATIENTS

Brent McNew
Healthcare and Public Health Research and Management

Background/Problem:
Ventilator-associated pneumonia (VAP) is a ubiquitous threat to the critically-ill patient. Recurrent VAP is common.

Objectives:
To use patient demographics and initial VAP episode microbiology as risk factors for recurrent VAP.

Methods and Materials:
From 9/01/07 to 8/06/08, 728 trauma patients had VAP diagnosed by bronchoalveolar lavage (BAL ≥10 cfu/mL). Recurrent VAP was defined as multiple positive BAL cultures with ≥ 24 hours between cultures. Variables of interest were compared by pathogen using the rank-sum test (continuous) or exact test (dichotomous).

Results:
One hundred forty-six patients (20.1%) had recurrent VAP, with a median of 8.5 days between cultures (mean 10.9 days). Patient demographics (age, gender, Injury Severity Score) were not significantly associated with single vs. multiple VAP episodes, nor were multiple pathogens in the first culture. The presence of specific pathogens in the first episode was not a risk factor for recurrent VAP. In patients with at least two VAP episodes, pseudomonas or stenotrophomonas in the first episode was associated with increased incidence of the same organism suggesting potential treatment failure.

Conclusions:
1. The risk of recurrent VAP is not a function of patient demographics, the initial pathogen, or the presence of multiple pathogens in the first BAL.
2. Recurrent VAP, while common (20%), rarely results from treatment failure but rather the selection of a new organism. 3. Consequently, empiric antibiotic therapy for recurrent VAP should reflect the unit’s resistance pattern.

Acknowledgements:
Andres Rodriguez, Patrick R. Norris Ph.D., Judith M. Jenkins M.S.N., William P. Riordan, M.D.
BLOOD UTILIZATION IN PERCUTANEOUS CORONARY INTERVENTION WITH CORONARY ARTERY BYPASS GRAFT

Imani Orgill  
Healthcare and Public Health Research and Management

Background/Problem: Combining CABG surgery with PCI (hybrid) could reduce the number of surgical grafts required compared to CABG alone. One of the major drawbacks in combining PCI and CABG surgery is the potential for increased risk of bleeding due to the need for antiplatelets agents.

Objectives: To assess the effects on blood utilization of combining a coronary artery bypass graft (CABG) procedure with percutaneous coronary intervention (PCI).

Methods and Materials: The patient population for this retrospective study included all subjects who had undergone a CABG procedure with or without PCI within the period of April 2005- April 2006 at Vanderbilt University Medical Center. Preoperative, postoperative, and intraoperative data were analyzed from electronic medical records.

Results: This study included 190 patients. The CABG group included 126 (66%) patients; the hybrid group (PCI + CABG) included 64 (34%) patients. There was no significant difference between the rates of major postoperative complications, reoperation for bleeding, or in-hospital mortality for the two groups. There was a significant decrease of cardiopulmonary bypass times (p=0.025) and aortic clamp times (p=0.0009) in patients who underwent a hybrid procedure. Patients who underwent a hybrid procedure had significantly higher chest tube output (p=0.001) and also received significantly higher amount of blood transfusions at 48 hours (p=0.004).

Conclusions: Hybrid revascularization does not increase the rates of postoperative complications, reoperation for bleeding, or mortality. Fewer surgical grafts are required with lower cardiopulmonary bypass times and aortic clamp times. This is achieved at the cost of greater blood loss and increased utilization of blood products.

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Mentor(s) and Department:  
Ramanan Umakanthan, M.D., Natalia Solenkova, M.D., Marzia Leacche, M.D., and John G. Byrne, M.D., Department of Cardiac Surgery, Vanderbilt University Medical Center

INAPPROPRIATE DELAYS IN THE ED: EXAMINING A POTENTIAL CONSEQUENCE OF QUALITY MEASURES

Piotr Pilarski  
Healthcare and Public Health Research and Management

Background/Problem: Evidence-based practice in emergency departments (EDs) has increased, because insurers such as Medicare are rewarding better performance on quality measures. These quality measures, however, are relevant to only select chief complaints (CCs), e.g., CCs representing acute coronary syndrome (ACS) or pneumonia. Hospitals may treat patients presenting with these CCs faster to improve their performance on quality measures, but because resources are limited, patients presenting with other serious CCs may experience inappropriate delays.

Objectives: The researcher compared the times that two ED patient populations with distinct CCs wait before they are assigned a bed or receive care from a clinician.

Methods and Materials: We used de-identified data of 9,431 adult ED patient visits. Controlling for fifteen confounders, we compared wait times for patients with quality measure CCs (chest pain, dyspnea, cough) to those with other serious CCs (stroke, focal weakness, disturbances of sensation, altered mental status, altered behavior, abdominal pain, shock).

Results: Patients with other serious CCs had a statistically significant 0.82 relative hazard of time to bed assignment and a statistically significant 0.83 relative hazard of time to first physician order when compared to patients with quality measure CCs.

Conclusions: Despite controlling for patient-specific confounders (e.g., age, ACS flag status, acuity, vital signs) and ED-specific confounders (e.g., average acuity, number of patient boarders, occupancy rate), patients with other serious CCs experienced significantly longer wait times. These results suggest that quality measures are unintentionally influencing ED clinicians’ triage decisions, causing some patients to face inappropriate and potentially harmful delays.

Acknowledgements: I would like to thank Caroline Cecot, Dominik Aronsky, and Sally Santen for their assistance with this project.

Mentor(s) and Department:  
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THE EFFECTS OF SART GUIDELINES AND STATE-MANDATED INSURANCE COVERAGE ON IVF TRENDS

Daniel Sacks  
Healthcare and Public Health Research and Management

Background/Problem: The success of in vitro fertilization has been hampered by two overarching problems: staggering financial costs and sensational multiple birth rates. In an
effort to combat the economic burden, some states have enacted legislation mandating the coverage of fertility services for couples with insurance. Meanwhile, a joint taskforce of the ASRM and SART has attempted to curb rates of higher-order multiples by publishing guidelines suggesting transfers of fewer numbers of embryos.

Objectives:
This study examined the interaction of embryo transfer guidelines and insurance mandates on numbers of embryos transferred. It evaluated the hypothesis that adherence to guidelines was directly linked to the availability of comprehensive insurance coverage which reduces costs associated with IVF treatment.

Methods and Materials:
Statistical analyses were performed on de-identified data collected by SART, including all women who underwent IVF treatment at reporting centers in the U.S. between 2004 and 2006.

Results:
Age and day of transfer were the most important predictors of the number of embryos transferred. Both the ASRM guidelines and state mandates were extremely significant (p<.001) as well.

Conclusions:
Even though both the guidelines and mandates were significantly associated with reduced numbers of embryos transferred, violations of the statistical model's assumptions made it not possible to conclude the causal effect of the guidelines. The transfer numbers are trending downward over time, and these two variables seem to be playing a role, but at this point, the size of the relationship cannot be concluded. There are still too many women receiving excessive numbers of embryos, and future studies need to look for ways to combat this problem.

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Mentor(s) and Department:
Esther Eisenberg, M.D., Department of Obstetrics and Gynecology, Vanderbilt University School of Medicine

CERVICAL SPINE INJURY IN PATIENTS TRANSPORTED BY AMBULANCE VERSUS PRIVATE AUTOMOBILE

James Teng
Healthcare and Public Health Research and Management

Background/Problem:
Prior studies of patients with cervical spine injuries (CSI) have identified high-risk groups based on demographics and mechanism of injury. However, none have compared the characteristics of patients transported to the emergency department (ED) by ambulance versus private vehicle.

Objectives:
To compare the injury patterns of CSI in patients transported to the ED by private vehicle versus ambulance.

Methods and Materials:
The researcher conducted a multicenter, retrospective, study of consecutive patients evaluated for CSI at three hospitals in Fresno, CA between 1/1/2000 and 12/31/2007. Patients transferred from outside facilities or whose original injuries occurred prior to the study period were excluded. Structured data collection included demographics, mode of transport, mechanism of injury, imaging results, stability, and neurologic deficits. Descriptive statistics were calculated and compared using Chi square and t-tests, as appropriate.

Results:
Of the 1174 medical records reviewed, 456 were excluded, leaving a study group of 718. Of this study group, 671 (93%) were transported by ambulance and 47 (7%) by private vehicle. Those transported by private vehicle had more stable injuries (66% vs 40%, p=.001), but similar rates of neurologic deficit (32% vs 24%, p=.25), and more spinal cord injury without radiographic abnormality (SCIWORA) (19% vs 5%, p=.001).

Conclusions:
Results demonstrate that patients with CSI who present to the ED by private vehicle are more likely to have stable injuries, but have a surprisingly high incidence of neurologic deficit, especially SCIWORA.

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Mentor(s) and Department:
Tyler Barrett, M.D., Emergency Medicine, Vanderbilt University Medical Center
Laboratory-Based Biomedical Research

Experiences in the area of Laboratory Based Biomedical Research are focused on hypothesis-driven investigation in a laboratory environment. Each student becomes a successful member in an active research program and completes a clearly defined project. Full-time research is performed during the summer between the first and second years of medical school and includes a seminar series designed to highlight the interaction between basic and clinical investigation. Students prepare both written and oral reports of their progress.

“Directing the Lab-Based Emphasis area was quite an adventure for me and the 22 participating students. Watching and guiding students as they moved from being overwhelmed with the wealth of potential mentors and choice of projects into becoming an integral team member at the lab bench was certainly rewarding. Students soon began to share their experiences with each other while taking ownership and pride in their accomplishments. By the end of final spring semester, a great many students were making plans for national poster presentations and portions of manuscripts. Mentors even encouraged a few to put on the brakes and get back to class. A number of the lab-based students are now considering options for exploring a more in-depth research project during and additional year of medical training. All have come to realize that lab research can be challenging but equally rewarding. I am confident that every single student will read journal articles with a much greater appreciation for the behind-the-scenes effort and serendipity that goes into the discovery process that shapes the future of medicine.”

“Full-time research is performed during the summer between the first and second years of medical school and includes a seminar series designed to highlight the interacting between basic and clinical investigation.”

Lillian Nanney, Ph.D., is the director of Plastic Surgery Research Activities, Co-Director of the Skin Disease Research Center, and the Founder and Director of Vanderbilt’s Institutional Immunohistochemistry Core Laboratory. She directs efforts to study a broad spectrum of conditions ranging from poor or delayed skin repair (burns, chronic wounds, mouse models of injury) to undesirable hyper proliferative growth conditions that include malignancy. She teaches full-time in Medical Gross Anatomy course and was the 2005 award recipient for best teaching in a small group setting. Dr. Nanney’s contributions extend to the national level where she recently served as the national president of the Wound Healing Society.
JITTER AND SHIMMER ANALYSIS OF DISCRETE PHONATION TYPES IN AN EVOKED RABBIT PHONATION MODEL

Davood J. Abdollahian
Laboratory-Based Research

Background/Problem:
Rousseau et al have described an in vivo rabbit model to investigate the effects of vocal fold vibration on expression of matrix metalloproteinases, which play a key role in regulating vocal fold extracellular matrix composition. Because the effects of vocal fold vibration on tissue ultrastructural alterations ultimately depend on phonation output, further characterization of rabbit phonation is needed to accurately match phonation dose in future biochemical studies.

Objectives:
The purpose of the current study was to investigate the effects of increased airflow rate and increased stimulation current on cycle to cycle variation in phonation frequency (jitter) and cycle to cycle variation in phonation intensity (shimmer).

Methods and Materials:
Seven New Zealand White breeder rabbits were used for the in vivo model. KayPentax Computerized Speech Lab was used to record and digitize acoustic signals. Two separate one-way repeated measures analysis of variance (ANOVA) tests were used to investigate within subject differences in percent jitter and percent shimmer between modal, raised, and pressed phonation. The F test revealed a significant main effect (p<0.025), pairwise comparisons between modal, raised, and pressed phonations were examined with Fisher’s LSD.

Results:
Percent jitter was 3.55 (1.63 SD) during modal phonation, 5.35 (2.77 SD) during raised phonation, and 10.36 (4.29 SD) during pressed phonation. Percent shimmer was 10.58 (3.76 SD) during modal phonation, 14.92 (6.45 SD) during raised phonation, and 22.53 (8.02 SD) during pressed phonation. Results of one-way repeated measures ANOVA revealed a significant within subjects effect for percent jitter (p<0.004) and percent shimmer (p<0.011). Post hoc pairwise comparisons revealed that percent jitter and percent shimmer were significantly higher during pressed phonation compared to modal phonation (p=0.019 and p=0.025, respectively). Differences in percent jitter and percent shimmer between modal and raised phonation were not statistically significant.

Conclusions:
Improved understanding of factors that influence perturbation in the in-vivo phonation model may result in improved capabilities to match phonation dose across animals in future biochemical studies.

Acknowledgements:
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MICE ELECTROPHYSIOLOGY STUDIES: INVESTIGATING THE LINK BETWEEN GENES AND ARRHYTHMIAS

Nneamaka Barbara Agochukwu
Laboratory-Based Research

Background/Problem:
Previous and ongoing research is improving our understanding of the genetic basis for abnormalities in heart rhythm (arrhythmias). The researcher has been investigating the genetic basis of arrhythmias using invasive electrophysiology studies (EPS) in genetically engineered mice with mutations in the tropomin T gene. These mutations are analogous to human mutations in tropomin T that cause hypertrophic cardiomyopathy (HCM). HCM is characterized by myofibrillar disarray, commonly leading to hypertrophy of the left ventricular myocardium, and increased risk for sudden death due to ventricular arrhythmias at a young age.

Objectives:
The researcher studied mice expressing different tropomin T mutations that confer different degrees of Ca 2+ sensitization. The hypothesis that mutations which increase the degree of calcium sensitization would increase the risk of arrhythmias was tested.

Methods and Materials:
An EP study was done following RIIV cutdown. Pacing was done to induce arrhythmias, particularly ventricular tachycardia (VT). A drug challenge (isuprel) was done for each group of mice, and pacing repeated.

Results:
Of the 11 mice analyzed: 6 had the troponin T mutation I79N and 5 were non-transgenic littermates (NTG). I79N mice had inducible VT with an average duration of 5.33 seconds. The NTG mice had an average duration of 1 s. After isuprel, 179N mice had significantly more VT episodes over 0.5s induced with double extra stimuli compared to NTG littermates.

Conclusions:
Mice with the I79N troponin T mutation (the calcium sensitizing mutation) are more susceptible to ventricular tachycardia than NTG mice. Further studies in mice with other troponin T mutations that confer varying degrees of calcium sensitization are required.

Mentor(s) and Departments:
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EFFECT OF ENDOCRINE-SPECIFIC CTGF INACTIVATION ON β CELL PROLIFERATION

Andre Boustani
Laboratory-Based Research

Background/Problem:
In both Type I and Type II diabetes, functional β cell mass is dramatically decreased. Therefore, understanding the signaling that leads to β cell proliferation is important in developing therapies, such as growing β cells in culture for implantation, or creating pharmaceuticals that increase β cell mass. In previous studies, transgenic mice over-expressing the HNF6 transcription factor exhibited increased alpha cell proliferation, and decreased β cell proliferation and mass. With microarray analysis, these mice had a 2.5 fold decrease in Connective Tissue Growth Factor (CTGF), indicating that CTGF may be a downstream signal mediating HNF6 effects on β cell proliferation. Additionally, both CTGF global knockouts and CTGF heterozygous mice were found to have similar abnormalities in endocrine proliferation.
Vanderbilt University School of Medicine
EMPHASIS PROGRAM FORUM IV
MAY 2009

Objectives:
Three cell types are known to release CTGF in the pancreas: vascular endothelium, pancreatic ductal epithelium, and _ cells. Our goal was to determine the effect of _ cell-released CTGF on _ cell proliferation.

Methods and Materials:
An ngn3-Cre transgenic, CTGFCOIN/COIN mouse was created. These mice allow for conditional inactivation of CTGF specifically in endocrine cells. In this mouse line, _ cell proliferation was analyzed.

Results:
β cell proliferation was 0.87% in the control CTGFCOIN/COIN line, and 0.56% in the ngn3-Cre transgenic, CTGFCOIN/COIN line, with a p-value of 0.02.

Conclusions:
β cell-released CTGF plays a role in β cell proliferation. However, since the decrease in β cell proliferation in endocrine-specific CTGF inactivated mice was less than that in CTGF global knockout mice, alternate sources of CTGF may play a role in β cell proliferation as well.

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Michelle Guney, Vanderbilt Student Research Training Program in Diabetes and Endocrinology

Mentor(s) and Departments:
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ALTERNATIVE SPlicing OF THE CARDiac SODIUM CHANNEL GENE SCN5A

Andrea A. Brock
Laboratory-Based Research

Background/Problem:
Sudden infant death syndrome (SIDS) is a leading cause of infant mortality and mutations in genes responsible for the congenital long-QT syndrome (LQTS), an inherited cardiac arrhythmia that has been found in 10-15% of cases. Therefore, a significant fraction of SIDS victims have an inherited predisposition to cardiac arrhythmia. Among SIDS-associated LQTS gene mutations, 50% occur in the cardiac sodium channel gene, SCN5A. Two alternative spliced SCN5A forms are observed: inclusion of a glutamine at amino acid 1077 (+Q1077) and exclusion of this residue (-Q1077). Alternatively spliced forms of SCN5A are important because of the potential for change in the functional properties of the channel.

Objectives:
To quantify the differences in expression between +Q1077 and –Q1077 in fetal, infant, and adult heart tissue.

Methods and Materials:
RNA was extracted from frozen tissues and quality checked by agarose gel electrophoresis and UV spectrophotometry. We measured mRNA levels from fetal, infant, and adult samples with real-time polymerase chain reaction (RT-PCR) using two fluorescent TaqMan probes that differentiate between +Q1077 and –Q1077.

Results:
The +Q/-Q allele ratio was calculated as 1.85, 2.64 and 2.64 for fetal, infant, and adult respectively with statistical significance occurring between fetal vs. infant and fetal vs. adult groups.

Conclusions:
These findings indicate that SCN5A +Q1077 is the predominant form of the gene and that mRNA levels for these alternatively spliced products of SCN5A may be developmentally regulated.

Mentor(s) and Departments:
Alfred L. George Jr., M.D., Division of Genetic Medicine, Vanderbilt University School of Medicine

REHABILITATION OF BILATERALLY PARALYZED CANINE LARYNX WITH IMPLANTABLE STIMULATOR

Yash Choksi
Laboratory-Based Research

Background/Problem:
Bilateral stimulation of the posterior cricoarytenoid (PCA) muscles offers a physiologic approach to rehabilitate ventilation to a normal level in case of bilateral laryngeal paralysis.

Objectives:
The objective was to evaluate the safety and efficacy of a new generation stimulator in restoring glottal opening, ventilation, and exercise tolerance.

Methods and Materials:
Study Design: A prospective study in three canines over 10-19 months.

Results:
During the denervation phase, there was minimal ventilatory compromise and near normal exercise tolerance (12 minutes up to 8 mph). PCA stimulation produced only nominal abduction. During the reinnervation phase, synkinetic reinnervation became significant with narrowed passive airway and paradoxical closure of the glottis during hypercapnea. Animals were stridorous and could walk for only 1-2 minutes @ 4 mph. With the device activated, bilateral PCA stimulation increased glottal area from 100 mm2 to 300 mm2, even during hypercapnea, equaling that of a normally innervated animal. Exercise tolerance was normal. There was no evidence of aspiration during deglutition.

Conclusions:
This study demonstrates that severe ventilatory compromise only occurs following faulty reinnervation of laryngeal muscles. Bilateral PCA stimulation can result in complete rehabilitation of ventilation and exercise tolerance without impairment of swallowing.

Mentor(s) and Departments:
David Zealear, Ph.D., and Kenichiro Nomura, Ph.D., Department of Otolaryngology, Vanderbilt University Medical Center
NEUROPROTECTIVE EFFECTS OF DEXAMETHASONE IN HT-22 HIPPOCAMPAL NEURONS FOLLOWING RADIATION THERAPY

Calvin M. Cooper
Laboratory-Based Research

Background/Problem:
Radiation therapy can decrease the growth and size of a tumor by inducing apoptosis, but can be neurotoxic to certain regions of CNS. Studies have shown a dose-dependent decline in cognition following radiation therapy of the brain, thought to be due to neurotoxic effects of treatment on the hippocampus. Dexamethasone, a glucocorticoid analogue, has been shown to protect hippocampal neurons following periods of cell stress. Currently, no studies have assessed the potential protective effect Dexamethasone may have on hippocampal neurons following cranial radiation therapy.

Objectives:
Study the potential protective effects of Dexamethasone on hippocampal neurons following cranial radiation therapy.

Methods and Materials:
Clonogenic assays were performed using HT-22 murine hippocampal cells. Cells were treated with either 1 μM Dexamethasone (Dex) or equivalent volume of Phosphorylated Buffered Saline (PBS). Each group was exposed to x-ray radiation treatment. Colonies were grown and stained with methylene blue for counting. Similar experiments were performed using mouse pups, which were sacrificed following cranial radiation treatment; sections of hippocampus were prepared with H&E stain. Flow cytometry was used following Dex or PBS treatment, radiation, and Annexin-V staining.

Results:
Clonogenic assays were analyzed using Sigma Plot software, depicting greater clonal cell survival and colony numbers in Dex group. Hippocampal H&E sections displayed a decrease in predicted apoptosis following treatment with Dex. Flow cytometry showed greater numbers of apoptotic cells in control group.

Conclusions:
These preliminary studies show that Dexamethasone may exhibit protective effects on mouse hippocampal cells in culture or in vivo following radiation treatment.

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COMPARISON OF LIPID LOCALIZATION PATTERNS IN CEREBELLUM

Chris Eakins
Laboratory-Based Research

Background/Problem:
Advances in MALDI mass spectrometry have made possible the localization of molecular species in tissue by mapping discrete spectra to a two-dimensional coordinate plane, allowing the generation of high-resolution images. These techniques have demonstrated application in the identification of organizational patterns of numerous biomolecules. Newer applications have aimed to elucidate the spatial distribution of phospholipids.

Objectives:
Techniques of assessing phospholipid localization are suited to evaluate structural intricacies in the CNS and lipid-dense structures. Lipids represent approximately 50% dry-weight of the CNS, are integral in cell signaling, pathways, and structures, and are known to fluctuate in disease states. This study aims to identify patterns among phospholipid organization in normal mouse cerebellum. To assess the feasibility of employing a mouse model, these patterns were compared to those in cadaveric cerebellum samples.

Methods and Materials:
Snap-frozen mouse brain samples and cadaveric cerebellum samples were cut into 12μm-thick sagittal sections and thaw-mounted to gold MALDI-MS plates. 2,5-dihydrobenzoic acid was applied by dry-coating receptors, our lab isolated B lymphocytes from mouse pancreatic islets and used DNA sequencing to identify the light chain pairings producing islet-infiltrating B cells.

Objectives:
This study was conducted to create a mammalian expression vector containing one of the light chain gene sequences isolated from our transgenic NOD mouse, in order that it could be co-transfected into a hybridoma cell line along with the an anti-insulin heavy chain vector to reproduce the autoantibody driving islet infiltration.

Methods and Materials:
The wild-type, 5’ upstream segment of VK 8-24 was ligated to our specific VK 8-24 sequence, which contained antigen-driven mutations in CDRs-1 and -3. The VK 8-24 insert now needs to be transferred from a PGEM cloning vector to a mammalian expression vector, PAN 4621, that contains a CK coding region in order to produce an intact light chain protein. Two PAN vectors with different versions of the VK 8-24 gene will be constructed for comparison studies: one with only the CDR3 mutation, and another with mutations in CDR1 and CDR3.

Conclusions:
Using expression vectors to produce large quantities of autoantibodies will allow for the characterization of autoantigens targeted early on in the T1DM disease process, providing a better understanding of disease progression and permitting new therapeutic targets and approaches.

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Mentor(s) and Departments:
James W. Thomas, M.D., Department of Rheumatology, Vanderbilt University School of Medicine

CONSTRUCTION OF A MAMMALIAN EXPRESSION VECTOR TO PRODUCE AN AUTOANTIBODY LIGHT CHAIN.

Brian Cruz
Laboratory-Based Research

Background/Problem:
Invasion of pancreatic islets by B lymphocytes is an important precursor to the T-cell mediated destruction of beta cells that results in Type 1 Diabetes Mellitus (T1DM). Using transgenic non-obese diabetic (NOD) mice that constitutively express anti-insulin heavy chains in their B cell receptors, our lab isolated B lymphocytes from mouse pancreatic islets and used DNA sequencing to identify the light chain pairings producing islet-infiltrating B cells.

Objectives:
This study was conducted to create a mammalian expression vector containing one of the light chain gene sequences isolated from our transgenic NOD mouse, in order that it could be co-transfected into a hybridoma cell line along with the an anti-insulin heavy chain vector to reproduce the autoantibody driving islet infiltration.

Methods and Materials:
The wild-type, 5’ upstream segment of VK 8-24 was ligated to our specific VK 8-24 sequence, which contained antigen-driven mutations in CDRs-1 and -3. The VK 8-24 insert now needs to be transferred from a PGEM cloning vector to a mammalian expression vector, PAN 4621, that contains a CK coding region in order to produce an intact light chain protein. Two PAN vectors with different versions of the VK 8-24 gene will be constructed for comparison studies: one with only the CDR3 mutation, and another with mutations in CDR1 and CDR3.

Conclusions:
Using expression vectors to produce large quantities of autoantibodies will allow for the characterization of autoantigens targeted early on in the T1DM disease process, providing a better understanding of disease progression and permitting new therapeutic targets and approaches.

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Mentor(s) and Departments:
James W. Thomas, M.D., Department of Rheumatology, Vanderbilt University School of Medicine
technique, utilizing a 20μm sieve apparatus. Data was collected using a Bruker UltraFlex II MALDI TOF-TOF mass spectrometer in positive-ionization reflector mode, exploiting over-sampling technique. Resultant spectra, correlating to phospholipid species with MS signatures in 400-1400 m/z range, were analyzed by FlexImaging software.

Conclusions:
Phospholipid organization was clearly segregated among histologically areas identified as gray and white matter. Limited phospholipids were recognized to uniquely localize to tissue consistent with the granular cell layer. Similarities were observed among phospholipid distribution in mouse and cadaveric samples, suggesting the mouse provides a model in which study of phospholipid organization can proceed.

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Mentor(s) and Departments:
Richard Caprioli, Ph.D., Department of Biochemistry, Vanderbilt University School of Medicine

MICROFLUIDIC FLOW CYTOMETER FOR COUNTING CD4+ T CELLS

Mark Fritz
Laboratory-Based Research

Background/Problem:
Physicians around the world routinely get CD4+ T-cell counts in their HIV patients to monitor treatment and to ascertain when to commence antiretroviral therapy. Flow cytometers currently perform this function but they have size, power, upkeep and versatility limitations that keep them from being at the bedside and in large parts of the developing world.

Objectives:
To research polydimethylsiloxane (PDMS) microfluidic devices and different cell staining techniques with Quantum dots (QD) to evaluate their clinical usefulness in counting CD4+ T-cells and providing a ratio of CD4+/CD8+ with the objective of making a cheap, small, easy-to-operate, easy-to-service microfluidic flow cytometer.

Methods and Materials:
Red Cross blood filter packs were purified to only T-cells through a FICOL protocol and magnetic separation step. These samples were then stained with either a QD-705 wavelength with CD3 antibody linking it to any T-cell present, or a similar QD cocktail. The stained cells were then split between those tested by the gold-standard FACSAria flow cytometer in the lab and those taken to custom PDMS microfluidic devices to determine whether they could be counted and analyzed further.

Results:
The cells have been staining well according to the gold-standard FACSAria, and the Qdot surface stains have been visualized with laser light excitation and photo-multiplier tube detection. Research is still ongoing at this point.

Conclusions:
The visualization of Quantum Dot surface stains with our first device holds promise for the already cheap and small technology of microfluidics. Research is ongoing at this point.

Mentor(s) and Departments:
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EVALUATION OF VIABILITY AND DIFFERENTIATION OF OSTEOPROGENITOR CELLS SEEDED ON BONE/POLYMER COMPOSITE

Nikita Gupta
Laboratory-Based Research

Background/Problem:
Bone healing mediated by polymer scaffolds holds substantial promise for the treatment of various forms of bone defects, including osteoporotic and vertebral compression fractures. An injectable, compression molded composite of 25% polyurethane (lysine methyl ester triisocyante and polyacaprolactone polyol) with 75% mineralized bone particle (75% mineral and 25% organic matrix) achieves mechanical properties similar to bone and bioresorbs in vivo.

Objectives:
It is predicted that surface demineralization of the bone/polymer composites will enhance an osteoconductive environment for increased cell attachment, proliferation, and differentiation.

Methods and Materials:
MC3T3-E1 mouse osteblast progenitor cells were cultured on the composites and treated with viability/cytotoxicity staining at 48 hours to determine attachment and viability. Alkaline phosphates assays were performed on MC3T3-E1 cells cultured on the composites at several time points over three weeks to determine differentiation to osteoblasts.

Conclusions:
Results and conclusions are pending.

Mentor(s) and Departments:
Scott Guelcher, Ph.D., Department of Chemical Engineering, Vanderbilt University

INVESTIGATION OF IL-8 INVOLVEMENT IN THE PATHOGENESIS OF GLAUCOMA

Pimkwan Jaru-ampornpan
Laboratory-Based Research

Background/Problem:
The final pathway of glaucoma is retinal ganglion cell (RGC) death. Tissue hypoxia has been proposed as an important factor contributing to RGC death. We have recently shown that interleukin-8 (IL-8) is elevated in glaucomatous aqueous humor.

Objectives:
To investigate IL-8 induction by hypoxia.

Methods and Materials:
An in vitro hypoxic experiment was performed using human anterior segment explant model. Each explant was divided equally into six pieces and was cultured separately in a tissue media under different conditions. A hypoxic environment was created by adjusting the CO2 and N2 contents of the incubator. An anoxic environment was created using BD GasPak Anaerobe Pouch System. Supernatants were collected before and after the induction. IL-8 induction was tested at mRNA level by real-time PCR and at protein level by Western blot. Statistical analysis was performed with t-test.
Results:
IL-8 mRNA induction was detected after 24 hours under anoxic condition (mean fold change = 4.95; n=7; p=0.028). The induction was also statistically significant after 48 hours under hypoxic condition (mean fold change = 5.60; n = 7; p=0.021). IL-8 protein elevation was detected after 48-hour incubation under hypoxic condition.

Conclusions:
IL-8 mRNA and protein productions are significantly induced by acute tissue hypoxia in vitro. Validation of this finding using cell culture model as well as investigation of IL-8 effects in the eye is currently being investigated in our lab.

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Mentor(s) and Departments:
Rachel Kuchtey, M.D., Ph.D., Department of Ophthalmology, Vanderbilt Eye Institute, Vanderbilt University Medical Center

DETECTION OF THE 4977 BP “COMMON DELETION” IN THE MITOCHONDRIAL DNA OF SEBORRHEIC KERATOSES

David P. Johnson
Laboratory-Based Research

Background/Problem:
Seborrheic keratoses (SK) are benign skin lesions commonly seen in older patients and are a common source of referrals to dermatologists to rule out malignancy. These benign growths have the potential to serve as a model for age-related neoplasia, but few studies have been performed to ascertain their genetics and etiology. Evidence shows that mitochondrial DNA (mtDNA) mutations, particularly the 4977 bp “common deletion,” are associated with photaging. Analysis of mtDNA mutations in SK may provide evidence of the relationship of this lesion with ultraviolet light exposure.

Objectives:
Evaluate the mtDNA of SK specimens for the presence of mtDNA point mutations and the 4977 bp deletion.

Methods and Materials:
mtDNA was extracted from 19 SK excision and paired blood control samples. Temperature gradient capillary electrophoresis (TGCE), a high-throughput mutation detection technique, was used to detect mtDNA differences between SK and paired controls. mtDNA deletions were analyzed by PCR amplifying the mtDNA using primers which spanned the deletion breakpoints in order to amplify species containing the deletion which could then be detected on an agarose gel.

Results:
The 4977 bp deletion was identified in 6 of 19 SK samples and none of the paired controls. TGCE results did not identify any mtDNA changes between SK and paired controls.

Conclusions:
Our results suggest that the 4977 bp deletion, which is associated UVA exposure, is also associated with SK indicating a role of UV light in SK etiology. Furthermore, the accumulation of mtDNA deletions in SK may promote the increased proliferation of keratinocytes that is characteristic of this condition.
DIFFERENTIAL REGULATION OF NAKED1 AND NAKED2 IN HUMAN COLORECTAL CANCER

Annie Y. Liu
Laboratory-Based Research

Background/Problem:
Naked1 and Naked2 are vertebrate orthologs of Naked cuticle, which was initially identified as an inducible antagonist of canonical Wnt signaling in Drosophila. Misregulation of Wnt signaling can cause degenerative diseases and cancers. Specifically, mutation of the critical Wnt negative regulator APC is associated with 80% of colorectal cancers, which are the second leading cause of cancer deaths in the United States.

Objectives:
To characterize the roles of Naked1 and Naked2 in tumorigenesis of colonic epithelium

Methods and Materials:
Western blotting and RT-PCR were used to examine expression of Naked1 and Naked2 in the SW480 parental and vector cell lines (derived from a human colon adenocarcinoma with mutant APC) and the non-transformed SW480.APC cell line stably expressing wild-type APC. Western blotting for Naked 2 was performed on human colon adenoma and carcinoma samples and normal adjacent mucosa controls.

Results:
The SW480 parental and vector cell lines exhibited high levels of Naked1 and low levels of Naked2; conversely, the SW480.APC cell line had high levels of Naked2 and low levels of Naked1. Ten of 16 human carcinoma samples demonstrated downregulation of Naked2 compared to adjacent normal mucosa samples, yet none of the 6 adenoma samples demonstrated any downregulation of Naked2.

Conclusions:
The upregulation of Naked1, whose levels are known to be elevated in colon adenomas, may be an earlier event in tumorigenesis than the downregulation of Naked2, whose levels are maintained in adenomas but decreased in carcinomas. Ongoing studies are being performed to characterize the differential regulation of Naked1 and Naked2 in normal and neoplastic colonic epithelium.

Acknowledgements:
I would especially like to thank my mentor, Dr. Robert Coffey, for his guidance and support. I would also like to thank Cunxi Li, Wei Ding, and the members of the Coffey lab for their assistance on this project. This work was supported by grants from the National Cancer Institute to Robert Coffey, from the GI Special Program of Research Excellence to Robert Coffey, from the Mouse Models of Human Cancers Consortium to Robert Coffey, and from the National Institutes of Health to Larry Swift.

Mentor(s) and Departments:
Robert J. Coffey, M.D., Department of Medicine, Department of Cell and Developmental Biology, Epithelial Biology Center

ROLE OF SIRT-1 AND NF-KB IN OSTEOBLAST PROLIFERATION AND DIFFERENTIATION

Melissa Makar
Laboratory-Based Research

Background/Problem:
Understanding how gene expression regulates age-related bone loss is a major area of interest. SIRT-1, a conserved histone deacetylase, may play a role in regulating bone mass as we age by interacting with several transcription factors. These include NF-kB, a ubiquitous transcription factor, which SIRT-1 inactivates to block the expression of NF-kB target genes.

Objectives:
We hypothesize that age-related bone loss is explained in part by a decreasing expression of SIRT-1 that results in enhanced NF-kB activity and decreased osteoblast proliferation and differentiation.

Methods and Materials:
To test this hypothesis, we verified the expression of SIRT-1 in osteoblasts with reverse transcriptase PCR and immunohistochemistry. We performed Western blots for SIRT-1 and NF-kB to verify protein expression. Next, we blocked NF-kB activity in osteoblasts and quantified the number of cells by measuring the amount of BrdU, a fluorescent thymidine competitor incorporated into cellular DNA.

Results:
In support of the hypothesis, an increase in cell proliferation over control was seen in the cells treated with an NF-kB blocker. These results correlate with separate osteoblast SIRT-1 knockout mice studies, which resulted in decreased bone volume over control mice. In light of our theory, this bone phenotype may be explained by an increased NF-kB activity seen with decreased SIRT-1 expression.

Conclusions:
Future experiments include creating transgenic mice that over express SIRT-1 in their osteoblasts and characterizing their bone to see if they are protected against age-related bone loss. In conclusion, through ongoing research, we are gaining a better understanding of how bone mass is genetically regulated over time.

Acknowledgements:
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Mentor(s) and Departments:
Florent Elefteriou, Ph.D., Center for Bone Biology, Clinical Pharmacology Division, Department of Medicine, Vanderbilt University School of Medicine

INVESTIGATING THE POTENTIAL USE OF RADIATION AND ZEBRAFISH VASCULATURE DEVELOPMENT IN A NOVEL DRUG SCREEN

Lauren R. Mitchell
Laboratory-Based Research

Background/Problem:
The use of zebrafish embryos as a model for screening novel radiomodifiers has previously been proposed but focused largely on gross morphological changes and neglected to investigate vasculature.

Objectives:
The purpose of this experiment is to analyze the effects of radiation and radiomodifiers on the formation of zebrafish vasculature and determine the validity of such a model for use as a drug screen.

Methods and Materials:
Five to ten embryos were placed in the wells of 24-well plates. Embryos were suspended in a 1mL solution of 0.5% DMSO, 5µM AT-101, a known radiosensitizer, or 4mMol amifostine, a known radioprotector, dissolved in PTU. Embryos received 0-40Gy irradiation within 30 minutes of drug exposure and were left in solution. They were evaluated 24 and 48 hours later.
post-radiation for changes in intersegmental vessels (ISVs.) Experiments were performed at several developmental stages.

Results:
Radiation was found to significantly affect zebrafish vascular development. Effects were most pronounced when embryos were radiated at the ten-somite stage (14 hr.) ISVs were shortened or missing and formed early anastomoses. Effects of AT-101 were prominent at lower doses of radiation (10Gy) and resulted in larger numbers of embryos to lack ISVs altogether. Amifostine effects were notable at higher doses of radiation (25Gy) and resulted in fewer embryos to lack ISVs and fewer deaths.

Conclusions:
This study concluded that zebrafish embryo vasculature would be an adequate model for a radiomodifier drug screen. However, different conditions may need to be established to screen for radiosensitizers and radioprotectors as effects are noted at different levels of radiation.

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Mentor(s) and Departments:
Bo Lu, M.D., Ph.D., Department of Radiation Oncology and Tao Zhong, Ph.D., Department of Cell and Developmental Biology, Vanderbilt University School of Medicine

LMO2 OVEREXPRESSION IN T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

Philipose Mulugeta
Laboratory-Based Research

Background/Problem:
LIM-domain-only-2 (LMO2) plays an important role in hematopoietic stem cell development and T-cell leukemia pathogenesis. LMO2 is expressed at the double negative (DN) stages of T-cell development, specifically DN2 and is overexpressed in approximately 50% of all human T-cell acute lymphoblastic leukemias (T-ALL). We created LMO2 transgenic mice that develop T-ALL with a median survival of 210 days and may indicate potential mechanisms for the T-cell differentiation block seen in many T-ALL patients. The failure to suppress CD4 expression could be associated with the activation of apoptotic pathways.

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Mentor(s) and Departments:
Utpal P. Dave, M.D., Division of Hematology Oncology, Vanderbilt University Medical Center

NOVEL SMALL MOLECULES REGULATE CARDIOMYOCYTE DEVELOPMENT BY OPPOSING WNT SIGNALING

Eric J. Rellinger
Laboratory-Based Research

Background/Problem:
Declines in cardiomyocyte populations following myocardial infarction predisposes afflicted individuals to sequelae, such as heart failure. Efforts to repopulate infarcted myocardium by stem cell transplantation have yielded modest benefits, demonstrating the need to develop strategies to enhance cellular differentiation towards a cardiac lineage.

Objectives:
Our primary goal was to identify and characterize small molecule modulators of cardiomyocyte development using a novel, phenotype-based screening assay in zebrafish.

Methods and Materials:
We conducted a chemical screen to identify compounds that modulate heart size using transgenic zebrafish embryos featuring EGFP expression in embryonic hearts. Active compounds were characterized in zebrafish to determine their mechanism of myocardial expansion, developmental period of efficacy, and target pathway. Parallel studies were conducted using murine embryonic stem cells to assess whether compound activity was conserved in mammals.

Results:
Three structurally-related compounds (Cardionogen A-C) strikingly increased zebrafish heart size in our assay. Cardionogen treatment increases cardiomyocyte numbers by expanding cardiac progenitor cell domains. In both zebrafish embryos and mouse embryonic stem cells, Cardionogen treatment after gastrulation promotes cardiogenesis, whereas treatment before gastrulation inhibits heart specification. This biphasic pattern of activity inversely resembles the role of Wnt/β-catenin signaling in cardiac development. Cardionogen-induced effects are antagonized by increasing Wnt/β-catenin signaling. We have also demonstrated that Cardionogen inhibits β-catenin/T cell factor-mediated transcription and can rescue heart phenotypes induced by wnt8 overexpression.

Conclusions:
Cardionogen modulates cardiomyocyte development by opposing Wnt/β-catenin signaling. Given the roles of Wnt signaling in regeneration, stem cell formation, and cancer progression, Cardionogen may have therapeutic applications for heart disease and cancer.

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EMPHASIS PROGRAM FORUM IV
MAY 2009


Mentor(s) and Departments:
Tao Zhang, Ph.D., Department of Cardiovascular Medicine, Vanderbilt University Medical Center

VALPROIC ACID PROTECTS HIPPOCAMPAL NEURONS FROM RADIOTOXICITY IN VITRO AND IN VIVO.

Kyle R. Sweeney
Laboratory-Based Research

Background/Problem:
Neurocognitive deficits follow cranial irradiation due to apoptosis of hippocampal neurons. Our earlier studies show that lithium prevents radiation-induced apoptosis in hippocampal neurons and improved cognitive performance in mice via inactivation of GSK-3β. Lithium and Valproate (VPA), a histone deacetylase (HDAC) inhibitor, have been shown to be neuroprotectors against various insults.

Objectives:
To demonstrate the neuroprotective effects of VPA in irradiated hippocampal neurons.

Methods and Materials:
Immortalized mouse hippocampal neurons (HT-22) were used for in vitro studies. Clonogenic survival assays were used to evaluate the role of VPA in cell survival. Apoptosis was measured by AnnexinV assays. Cell cycle analysis was performed using PI staining. Protein changes were analyzed by subjecting cell lysates to immunoblotting. Seven-day old C57BL6 pups were used to study apoptosis in vivo.

Results:
24 hour pretreatment of HT-22 cells with VPA showed accumulation of hyperacetylated histone H4 in a dose-dependent manner and increased phosphorylation of GSK-3β (inactivation) and accumulation/stabilization of β-catenin. Clonogenic survival assays showed pretreatment of HT-22 with 0.6 mM VPA for 7 days before irradiation resulted in significantly increased cell survival as compared to untreated, irradiated cells. This was not observed in glioblastoma cell lines. Mouse pups pretreated with VPA (400mg/Kg) followed by 7Gy radiation showed decreased pyknotic nuclei in the hippocampus compared to animals receiving radiation alone.

Conclusions:
VPA protects hippocampal neurons from radiation-induced damage in cell culture and animal models. The molecular mechanism could involve inhibition of HDAC and GSK-3β. VPA could be a novel therapy for preventing neurocognitive deficits resulting from cranial irradiation.

Mentor(s) and Departments:
Kevin B. Wise
Laboratory-Based Research

EXPERIMENTAL STUDY ON TARGETING OF NON-SMALL LUNG CANCER CELL

Vinod Varki
Laboratory-Based Research

Background/Problem:
Targeted cancer therapies are a novel way to potentially treat and cure cancers without side effects of radiation or chemotherapy treatment alone. Biological agents represent a novel class of cancer therapeutics because of less normal tissue toxicity. Dr. Hallahan’s laboratory has previously demonstrated that irradiation of tumor cells and their vasculature can result in the presentation of cell surface neo-antigens. These irradiation-inducible antigens can serve as potential targets for therapeutic antibodies, radio-immunoconjugates, and targeted drug delivery molecules.

Objectives:
To select a monoclonal antibody that binds to Non-Small Lung Cancer Cell (H23) and induces an immune response after radiation.

Methods and Materials:
Five purified antibodies were screened by immuno-histochemistry. One antibody was the candidate that was used on the H23 cell line. Phagocytosis experiments were performed in vitro, imaging studies were performed in vivo in addition to an Elispot.

Results:
The 7D4 antibody showed the strongest binding after radiation treatment in immuno-histochemistry studies. Dendritic cells phagocytosed the H23 cells after radiation treatment with 7D4. Imaging studies in mice showed binding of the antibody after radiation treatment compared to other IR dosages and the non-radiated tumor cell. Finally, an ELISOPOT experiment on the H23 cell showed a strong immune response with an increased secretion of Interferon Gamma from the lymphocytes after radiation treatment compared to other IR dosages and the non-radiated H23 cell line.

Conclusions:
The 7D4 antibody showed binding to H23 in vitro and in vivo by IHC and mouse imaging respectively. An immune response was qualitatively shown in the phagocytosis experiment and quantitatively measured for immune response in ELIPSOT for IFN-gamma.

Acknowledgements:
Emphasis Program

Mentor(s) and Departments:
Dennis Hallahan, M.D., and Heping Yan, M.D., Department of Radiation Oncology, Vanderbilt University School of Medicine

DETECTION AND QUANTIFICATION OF APELIN IN THE VITREOUS HUMOR OF PATIENTS WITH PROLIFERATIVE DIABETIC RETINOPATHY

Kevin B. Wise
Laboratory-Based Research

Background/Problem:
Proliferative diabetic retinopathy (PDR) is an increasingly common cause of vision loss worldwide resulting from abnormal growth of blood vessels in the retina. Identification of growth factors associated with retinal angiogenesis may lead to rational anti-angiogenic therapy. The Recchia lab has demonstrated significantly increased expression of the gene apelin (coding for the angiotensin type 2-like receptor 1 ligand) in two rodent models of oxygen-induced proliferative retinopathy. Apelin promotes angiogenesis in vitro in retinal and choroidal endothelial cells and is required for normal vasculogenesis in other organ systems.

Objectives:
To detect and quantify the level of apelin in human vitreous to determine if higher levels are associated with PDR.
**Methods and Materials:**
Undiluted vitreous and serum samples were obtained from patients undergoing vitreoretinal surgery for PDR and from non-diabetic patients undergoing surgery for non-vascular disease. The concentration of apelin in these samples was measured in duplicate by ELISA. Concentrations were compared using the Wilcoxon two-sample test.

**Results:**
Patients with PDR (n=15) had a mean apelin concentration of 40.2 pg/mL, while non-diabetic patients (n=26) had a mean concentration of 29.6 pg/mL (p=0.066). Serum concentrations of apelin did not differ significantly between the PDR (358 pg/mL) and non-diabetic (321 pg/mL; p=0.62) groups.

**Conclusions:**
Vitreous levels of apelin were elevated in patients with PDR. Serum levels of apelin in PDR patients and non-diabetic patients were similar, suggesting that apelin may be synthesized and released by ischemic retina. As apelin may play a role in retinal angiogenesis, its mechanism of action and potential as a therapeutic target warrant further study.

**Acknowledgements:**
Franco Recchia, M.D., Lili Xu, M.D., Ph.D., Susan Yanni, Josh Barnett, and Hassanain Toma, M.D.

**Mentor(s) and Departments:**
Franco Recchia, M.D., Division of Vitreoretinal Disease and Surgery, Vanderbilt Eye Institute, Department of Ophthalmology and Visual Sciences, Vanderbilt University Medical Center

**AGE-RELATED FIBROBLAST RESPONSES TO VOCAL FOLD INJURY**

Mi Jin Yoo  
*Laboratory-Based Research*

**Background/Problem:**
Age and injury related voice changes result from a disruption in the normal balance of the vocal fold extracellular matrix (ECM). Previous studies have revealed dense collagen deposition and reduced hyaluronan in the aged and scarred vocal fold. The change in cellular production of ECM in the aged vocal fold after injury is not well understood.

**Objectives:**
To investigate gene expression from vocal fold fibroblasts obtained from young and aged rats following vocal fold injury.

**Methods and Materials:**
Twelve 2-month old (young) and twelve 18-month old (aged) Sprague-Dawley rats were used in this study. Young and aged rats were further divided into two groups (control and injury). Rats in the injury group received bilateral vocal fold injury and were euthanized two months after injury. Rats in the control group were painlessly sacrificed without vocal fold injury. Fibroblast cultures were established from harvested vocal fold specimens. Real-time PCR was used to quantify messenger RNA expression of hyaluronan synthase (HAS)-2, -3 and matrix metalloproteinase (MMP)-2, -9 from second passage fibroblast cultures.

**Results:**
Fibroblasts from young injured rat vocal folds showed decreased HAS-2 and MMP expression after injury. Further understanding of the scarring and aging process at the molecular level may lead to novel treatments for age and injury related changes of the vocal fold.

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**Mentor(s) and Departments:**
Bernard Rousseau, Ph.D., Department of Otolaryngology, Vanderbilt University School of Medicine
Law & Policy

Medicine is influenced in every aspect of its practice by law and policy. The goal of the Law and Policy emphasis area is to help students understand more fully the complexity of these interactions and to give them tools to participate effectively in these arenas. All of the students enrolled in an interdisciplinary course with law and divinity students explored the intersections law, ethics and medicine and all were instructed in basic methods of legal research. Their actual projects used a variety of methods and ranged across numerous topics. Many engaged in qualitative and survey research to obtain information that could inform policy decisions.

Students in this area have pursued an array of projects, from working directly with Congressmen and federal and state health officials to doing empirical projects that directly inform the legislative process and other areas of health policy. Students have presented their work at national meetings and to health policy makers. Many of the students have gone on to pursue additional degrees in areas such as law and business.

Students interested in the law and policy area are strongly urged to begin identifying a project and mentor early.

This process works best if you bring some ideas of interests and possible contacts. In most cases, you will be working primarily with a person outside of Vanderbilt; when this occurs, you will have a secondary mentor in the program.

Other parts of this program include: 1) an interdisciplinary course in the spring of the first year students from the law and divinity schools, which will expose you to different ways of approaching medical ethics and provide you with basic skills in legal research, and 2) an opportunity to present your project to your fellow students, which has turned out to be a great experience for students and faculty.

This program is directed by Joshua Perry, J.D., M.T.S., in the Center for Biomedical Ethics and Society.

Josh Perry, J.D., M.T.S. is an assistant professor in the Center for Biomedical Ethics and Society. Professor Perry’s teaching, research, writing and service are intentionally interdisciplinary with a broad focus on the areas of bioethics, clinical medical ethics, health law/policy, medical/legal professionalism, and moral decision making. His research explores how tensions between personal and professional values in the lives of lawyers impact upon identity formation and moral decision making, as well as related public policy “biopolitical” issues arising in dilemmas where legal, medical, ethical, and religious issues intersect. His work in these areas has been published in Annals of Internal Medicine, Health Matrix: Journal of Law-Medicine, Journal of Legal Medicine, DePaul Journal of Health Care Law, and Tennessee Medicine. In addition to teaching graduate and undergraduate courses at the law and medical schools and the College of Arts and Sciences, Professor Perry also serves as a member of the Clinical Ethics Consultation team and as a member of the VUMC Ethics Committee.

“I am confident that the students know more now about the setting in which medicine is practiced, and that they will be more effective advocates in the future as a result.” Ellen Wright Clayton, Co-director of the Center for Biomedical Ethics and Society
IDENTIFYING RESOURCES AND CHALLENGES FOR INITIATING MLP’S FROM A OBSERVATIONAL CROSS-COUNTRY ANALYSIS

Anjali Deshmukh
Law and Policy

Brief Description:
Analyzing a national cross section of Medical Legal Partnerships (MLP) through internships revealed common problems and unique solutions, which are summarized in this research to help new partnerships like Vanderbilt’s MLP.

Summary:
The basic Medical Legal Partnership (MLP) model of lawyers joining medical teams to better serve patients is consistent across the nation. However, each partnership faces differences in resources and challenges and thus requires different approaches to solving problems. Initiating and continuing a MLP is difficult, and the successes of a partnership fluctuates as these circumstances change over time. Our objective was to examine more established MLP partnerships in an observational cross-sectional study and identify successful strategies and techniques to cope with challenges faced by a newer partnership with which the investigator was associated. Through a series of internships and interviews, the investigator had an opportunity to observe and gain insights into the structure, internal mechanisms, and everyday functions of MLPs in various stages of development. The information from these case examples was analyzed to propose recommendations that could be generalized for new partnerships with individual variables.

Conclusions:
By further comparing turnover rates, number of staff, long-term funding potential, and number of hospitals served, we developed a series of policy recommendations that are currently being adopted by some MLPs. This information would be unquestionably beneficial for newly established partnerships that are struggling with similar issues.

Mentor(s) and Department:
Ellen Clayton and Josh Perry, Vanderbilt University School of Medicine, Jay Sicklick, Medical Legal Partnership Project (Hartford, CT) and Chay Sengkhounmany, Medical Legal Partnership (Nashville, TN)

THE ROAD TO USA UNIVERSAL HEALTHCARE: A STUDY OF CVD MANAGEMENT IN AUSTRALIA

Maher Salahi
Law and Policy

Brief Description:
With an uninsured rate exceeding 15%, the deteriorating United States (US) healthcare system must be reformed. Australia’s rarely studied system, on the other hand, is regarded as one of the best. Its services subsidize prescription drugs, physician visits, and medical procedures for everyone. Further, its population’s average life expectancy easily surpasses the US’s, while its per capita healthcare expenditure is half that of the US. This study is, therefore, aimed at exploring cardiovascular disease (CVD) management in Australia to suggest positive changes in our system for this and other expensive, chronic illnesses.

Summary:
The investigator spent nine weeks in Australia gauging its system’s strengths and weaknesses by conducting an exhaustive literature review, speaking to policy advisors and analysts, patients, physicians, and economists, and shadowing cardiologists and cardiac rehabilitation nurses in their practices. While Australia supports a low-cost universal healthcare system funded by income taxes, it is tarnished by inequitable access to care, long waiting lists, rising expenses, and a complicated set-up that few physicians, patients, or policy advisors understand. Prescription medications for cardiac disease are also expensive for the poor and many cannot afford them. Conversely, the US utilizes state-of-the-art technology at the expense of higher costs, noticeable inefficiencies, and large discrepancies in CVD care.

Conclusions:
Despite the problems in Australia’s healthcare system, it is a good model to consider in the US for CVD and chronic illness management due to its healthy public-private insurance mix, its competitive healthcare environment, its coverage for all, and its partial pharmaceutical government subsidies.

Acknowledgements:
Dr. Ellen Clayton for her support and mentorship before, during, and after the investigator’s stay in Australia. Dr. Lesley Russell and the rest of the staff at the University of Sydney for their tireless efforts in making the investigator comfortable in Australia. Finally, the Overall Fellowship, without which the experience in Australia would not have been the same.

Mentor(s) and Department:
Dr. Ellen Clayton, Department of Medicine, Vanderbilt University School of Medicine and Dr. Lesley Russell, Menzies Centre for Health Policy at the University of Sydney.
Emphasis experiences in the Medical Education area are designed to introduce students to the theory and practice of learning and teaching in medicine. Students are provided an overview of current research describing how medical students, residents, practicing physicians and patients learn as well as information about effective teaching strategies. In addition, each student has the opportunity to develop a project in an area of interest. Projects can include research or curriculum development.

Educational experiences will focus on, but will not be limited to, addressing the following questions:

1. How can students develop skills to reflect on their own performance as a part of a personal approach to lifelong learning and continuing professional development that can be used throughout their medical careers?
2. What teaching strategies help medical students, residents, practicing physicians, and patients learn?
3. How are research studies in medical education conducted and research findings interpreted?
4. How is curriculum developed and evaluated in medical school and residency settings?

“Working with students in the Emphasis Program was one of the highlights of the past three years for me. It was an honor and privilege for me to watch and share their excitement and satisfaction as they worked through and accomplished their projects. I am looking forward to working with the students who choose the Medical Education area during this coming year.”

“Emphasis experiences in the Medical Education area are designed to introduce students to the theory and practice of learning and teaching in medicine.”

Don Moore, Ph.D. is a Professor of Medical Education and Administration, Director, Division of Continuing Medical Education at Vanderbilt University School of Medicine, and Director, Education and Evaluation, Graduate Medical Education. He has devoted a considerable amount of his professional career examining, writing and speaking about continuing medical education and a number of other related areas such as: practice-based CME, planning and assessing CME, and how Physicians learn. His research interests also include the role of CME in physician change, office systems for CME, and the impact of CME on health care outcomes.
**LABORATORY PRACTICES FOR THE DETECTION OF SHIGA TOXIN-PRODUCING E. COLI**

**Lane Crawford**  
*Medical Education*

**Brief Description:**  
We surveyed Tennessee laboratories to assess adherence to recommended protocol for STEC detection and to identify barriers to adherence.

**Summary:**  
Shiga toxin-producing E. coli (STEC) is an important cause of diarrheal illness and hemolytic-uremic syndrome. In the US, the most commonly isolated STEC serotype is O157:H7, but emerging non-O157 serotypes cause 20-50% of STEC infections. Currently, most laboratories screen for STEC by sorbitol-MacConkey agar culture (SMAC), which does not detect non-O157 serotypes. Rapid immunological Shiga toxin assays that detect all serotypes are available for clinical use. In 2006, the Centers for Disease Control (CDC) recommended that laboratories screen all specimens by toxin assay with simultaneous SMAC culture. Adherence to this protocol offers significant clinical and public health benefits. This study sought to describe current laboratory protocols for STEC detection in Tennessee and to identify factors influencing choice of protocol. Data was collected via scripted interview with microbiology supervisors. Of 130 targeted labs, we received 117 responses (90% response rate). Of the labs that performed stool cultures in house, only 81% screened all specimens for STEC. Of the labs that tested some or all specimens for STEC, 70% used SMAC alone, 7% used toxin assay alone, and only 22% used both tests, as recommended by the CDC. The most significant barriers to using toxin assay were lack of awareness about current recommendations, high cost, and less convenient fit with laboratory workflow. Results indicate that very few laboratories in Tennessee are adherent to recommended STEC detection protocol. Provider education will be key to improving adherence.

**Acknowledgements:**  
The authors thank Charlene M. Dewey, M.D., M.Ed., for serving as the Emphasis mentor throughout the project and with helping with survey design, Sean Moore, M.D., for collaboration on paper-writing, Emil Petrusa, Ph.D., for survey validation, Mario Davidson, Ph.D., for biostatistics advice, and John V. Williams, M.D., Natasha Halasa, M.D., and Alison Crawford for additional assistance.

**Mentors and Departments:**  
Charlene M. Dewey, M.D., M.Ed., Department of Medicine

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**ASSESSMENT OF PATIENT INTEREST IN AND KNOWLEDGE OF STIS AT A PUBLIC HEALTH CLINIC**

**Stamatios Dentino**  
*Medical Education*

**Brief Description:**  
Educating the public on sexually transmitted infections (STIs) and other women’s health issues continues to be a concern of health professionals. Research focuses on what aspects of STI education a patient population lacks. The purpose of this study was to determine areas of STI education patients are most interested in receiving and in which areas knowledge was lacking.

**Summary:**  
 Planned Parenthood of Hawaii (PPH) was consulted to identify which STIs were of most local concern. A 34-item survey included responses to interest in HPV, Herpes, Syphilis, Gonorrhea, and Chlamydia (1 = “none” to 7 = “a lot”) and “yes/no/not sure” responses about general knowledge and epidemiology. IRB approval, mutual indemnification, and an interinstitutional contract established. Two months were spent in the local PPH clinic surveying patients. Data was compiled and analyzed using StatView for Windows® statistical software. Patients (N=50) were most interested in information about HPV (M = 4.2) with statistically less interest in Syphilis (paired t-test p = .05) and Gonorrhea (p = .04). To determine knowledge level, correct answers were assigned values of “0” (correct), “1” (not sure), and “2” (incorrect). Patients knew the least about syphilis (M = .61) and most about HPV (M = .28). Lack of knowledge varied from disease to disease, with statistically significant differences between each STI except Chlamydia and Gonorrhea (paired t-test, a ≤ .05). Respondents had most knowledge of HPV while also expressing the greatest interest in learning more about it. They knew least about Syphilis, but expressed almost the least interest in knowing more. Such results can guide health professionals in tailoring specific educational programs to the interests of patients while also addressing areas about which they knew least.

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**Mentors and Departments:**  
James L. Bills, Ed.D., M.S., Medical Scientist Training Program, Vanderbilt University School of Medicine

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**FACULTY CAREER OPTIONS AT U.S. ALLOPATHIC MEDICAL SCHOOLS**

**Michelle Sullivan**  
*Medical Education*

**Brief Description:**  
This is a research project conducted in conjunction with the Association of American Medical Colleges (AAMC) to describe career options available to faculty at academic medical centers.

**Summary:**  
Faculty career options at U.S. medical schools have been changing over the last 30 years, particularly in regards to clinically-focused tracks and presumably due to the ever-changing pressures faced by academic medical centers. This study describes the career options currently available to faculty members in academic medicine. Information about career options were collected from medical school faculty manuals from 75 U.S. allopathic institutions. Medical schools, on average, offered 3.7 career options to their faculty members (range 1-6). Most of these career options were non-tenured. Overall, schools offered more research-focused career tracks than education- or clinically-focused tracks. However, all schools with three or more career options (n=63) offered a track where clinical service was the major professional activity. 26 institutions offered a track in which education/teaching was the major professional activity. Two thirds of schools (n=49) utilized modified titles for faculty pursuing non-tenure tracks. Schools which offered more career options were more likely to utilize these modified titles. The results of this study emphasize the great variation in faculty policies from one institution to the next. Medical school administrators might find the results of this study relevant in evaluating and comparing their own faculty policies. The results will also be informative to faculty members, residents, and medical students as they consider their career options in academic medicine.

**Mentors and Departments:**  
George V. Richard, Ph.D., Director, Careers in Medicine Program Association of American Medical Colleges (AAMC), Scott Rodgers, M.D., Associate Dean for Medical Student Affairs Vanderbilt University SOM
Medicine both shapes and is shaped by the larger society. The Medical Humanities provide ways of understanding how the interaction occurs, and how it affects individual health care and health policies. 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.
- Religion/spirituality provides strategies for appreciating the ways illness, suffering and death are interpreted by patients and their families and caregivers.

The humanities 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.

Students who select an Emphasis project in Medical Humanities will usually select a specific area of focus in order to achieve some degree of mastery and depth. However, programs of study that combine these areas may also be designed and additional focus area within the medical humanities may be open to students from time to time, depending on the availability of faculty mentors, electives within the medical curriculum or other courses in the university. In all cases, students will be encouraged to design a flexible program that best fits their interests and goals rather than a predetermined path.

During the first semester of VMS I, students will be exposed to the nature of humanities scholarship through lectures, seminars and individual meetings with potential mentors in each area described above. In the spring semester, students will meet with area director and members of the area committee to discuss their projects. At the end of spring semester, students will turn in an annotated bibliography covering the pertinent literature for their projects.

“A medical history can read like a detective story and a novel can become a moral laboratory, with the result that historical perspective, literary imagination, and ethical literacy can all contribute substantially to good doctoring.”

Mark J. Bliton, Ph.D. received his undergraduate degree in Philosophy and English from Allegheny College before studying Applied Philosophy at Bowling Green State University, OH and then becoming a student of Richard M. Zaner in the Center for Clinical and Research Ethics at Vanderbilt University. While working toward his PhD in the Department of Philosophy at Vanderbilt, Bliton also served as a Clinical Fellow in the Center as well as an Instructor of Medical Ethics in Vanderbilt’s School of Medicine. A faculty member of Vanderbilt University’s for Biomedical Ethics and Society, Bliton is an Associate Professor in the Department of Medicine. He has been a member of Vanderbilt University Medical Center’s Ethics Community since 1991. His work is now focused in the Monroe Carell, Jr. Children’s Hospital at Vanderbilt.
THE INFLUENCE OF MARY SHELLEY ON THE WORKS OF RICHARD SELZER

Kara Brown
Medical Humanities

Objectives:
The goal of this project was to explore the connection between Mary Shelley’s novel Frankenstein and Richard Selzer’s short story “Imelda.”

Brief Description:
By comparing themes and passages between the two texts, in addition to using personal interviews with Selzer, I proposed that Selzer was influenced by Shelley and that “Imelda” is his revision of Frankenstein.

Summary:
This project examines the influence of Mary Shelley on the works of Richard Selzer, in particular, his short story “Imelda.” A close reading of both texts with particular attention to the post-mortem operation in “Imelda” and the creation scene in Frankenstein reveals an overwhelming connection between the two texts. The post-mortem operation passage mimics the creation scene with respect to the Gothic imagery and the role of surgery to animate an inanimate being. Furthermore, undeniable similarities exist between the stories’ protagonists, Franciscur and Frankenstein, the role of women in both texts, the use of religion and science, and the presence of the Gothic in both works. However, there are important divergences between the two texts that not only lead to vastly different endings, but also reveal Selzer’s intentions in fashioning “Imelda” after Frankenstein. Using published interviews with Selzer, the author postulated that Selzer’s attachment to the surgical profession led him to deviate from Frankenstein’s conclusion and to write “Imelda” in order to humanize and defend the surgeon in response to the harsh critique of science Shelley delivered in Frankenstein.

Mentor(s) and Department:
Holly Tucker, Ph.D., Center for Medicine, Health and Society

ELECTRONIC HEALTH RECORDS AND THE PHYSICIAN-PATIENT RELATIONSHIP

Shane Magee
Medical Humanities

Objectives:
The goal of this study was to define points at which the electronic health record can influence the physician patient relationship.

Brief Description:
Interviews were conducted with heart attack patients admitted to Vanderbilt University Medical Center (VUMC) in order to analyze the effect of Vanderbilt’s electronic health records on the physician-patient relationship.

Summary:
Five patients admitted to VUMC with a first MI were interviewed in the hospital days s/p MI, 1 month s/p MI, 3 months s/p MI, and 6 months s/p MI, but only four have completed the second interview at the time of publication. The remaining interviews are scheduled for March/April. At the first interview, the patient was allowed to tell his/her story. At the following interview, a written narrative constructed from the transcript of the first interview was presented to the participant along with pieces of the EHR in order for the participant to respond to the differences between his/her view of what happened, the constructed narrative, and the EHR. Questions were designed to elicit responses concerning how the participants viewed electronic health records. The interviews were analyzed according to methods of grounded theory. Though the study is ongoing, preliminary analysis indicates that EHR plays a role in easing a patient’s fears for the future, enabling a means for controlling their situation, and a way to feel part of their own medical team. Unfortunately, the EHR also plays to a patient’s fear of becoming a statistic and the frightening idea that life can never return to "normal."

Mentor(s) and Department:
Mark Bliton, Center for Bioethics, Vanderbilt University


Ryan Darby
Medical Humanities

Objectives:
Examine the ethical issues in cognitive enhancement.

Brief Description:
A recent survey of Nature readers revealed that up to 40% of those who replied were using medications commonly used for cognitive enhancement. Of these, 50% were being obtained without a prescription for a medical disease. Subsequently, Greely et al (2008) have called for the responsible use of enhancement in normal individuals. The message is that the use of drugs for cognitive enhancement is not merely a philosophical thought experiment, but an actual problem that deserves careful consideration. First, ethical arguments against enhancement will be addressed. These arguments can be divided into two categories: issues dealing with the individual use of enhancement, such as maintaining autonomy and authenticity, and those dealing with the larger implications of a society accepting enhancement, including coercion to use enhancement and the creation of inequality. The author’s main thesis was that arguments against the individual use of enhancement can be overcome, provided there is autonomy of choice and accurate information on the costs and benefits of cognitive enhancing drugs. The author also argued that the extent to which enhancement will have negative effects on society depends more on the way that institutions apply these technologies than on the characteristics of the technologies themselves, and that these negative effects are the result of decreased autonomy for certain groups of persons. Finally, the author argued that enhancement is consistent with certain definitions of the role of medicine, and that medicine, as an institution, can help to regulate enhancement in a responsible manner.

Mentor(s) and Department:
Dr. Jeff Bishop, Associate Professor of Biomedical Ethics and Medicine, Vanderbilt University School of Medicine
The central goal of the Medical Scientist Training Program (MSTP) is to train leaders in academic medicine. Students are provided with an integrated curriculum comprising a strong core education in medicine and intensive training in scientific inquiry using a preceptor-oriented, problem-solving approach. MSTP students usually complete the first two years of Medical School, pursue graduate studies for three to four years, and then return to Medical School to complete the final two years of clinical training. The program enrolls 10-12 new students per year, each of whom receives a tuition scholarship and a stipend to cover living expenses. The MSTP is a joint endeavor between the Vanderbilt University School of Medicine and the Vanderbilt University Graduate School. Trainees fulfill all of the requirements for both the M.D. and Ph.D. degrees.

“The Emphasis program allows our MSTP students to complete three laboratory rotations and choose a mentor to guide the Ph.D. thesis research. This is an incredibly important experience 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.”

“Full-time research is performed during the summer between the first and second years of medical school and includes a seminar series designed to highlight the interaction between basic and clinical investigation.”
MTOR KINASE SIGNALING IN NEUROLOGICAL DISEASE

Eric A. Armour  
Medical Scientist Training Program

Background/Problem:  
The mTOR kinase signaling pathway has been implicated in the regulation of many cellular processes including cell growth, proliferation, motility, cell survival, gene transcription and protein synthesis. Given the multiple roles performed by the mTOR kinase, disruption of this pathway is likely to underlie multiple human diseases. The best characterized example of this is Tuberous Sclerosis Complex (TSC), a multiorgan disease found in approximately 1 in 6,000 live births and caused by a loss of function of either the TSC1 or TSC2 genes. Despite involvement of skin, heart, and kidneys, neurological aspects are usually the most severe due to a high prevalence of mental retardation, autism and epilepsy. Recent studies position the TSC genes as upstream regulators of mTOR and various tissues from these patients show highly increased levels of mTOR signaling. The precise role of the mTOR pathway in brain development remains unclear.

Objectives:  
To define the role of human TSC1 and TSC2 genes during both normal development and the pathogenesis of TSC, with a focus on the neurological component of the disease.

Methods and Materials:  
Primary fibroblast cultures were derived from skin biopsies of several patients with TSC. These cells were transfected with three key transcription factors, KLF4, OCT4 and SOX2 to generate induced pluripotent stem (iPS) cells. These cells will provide an in vitro model to study abnormalities of proliferation, cell size and neuronal differentiation.

Conclusions:  
Experiments are currently in progress. Pluripotency of these cells are being confirmed. Following confirmation, differentiation assays and mTOR dependence will be performed.

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Mentor(s) and Departments:  
Kevin Ess, Ph.D., Department of Neurology and Department of Pediatrics, Vanderbilt University School of Medicine

MECHANISMS OF REOVIRUS CELL ATTACHMENT: ROLE OF Σ1 LENGTH.

Magdalena Bokiej  
Medical Scientist Training Program

Background/Problem:  
Receptor recognition plays a vital role in viral tropism and constitutes the first step in viral infection. Cell-adhesion molecules and cell-surface carbohydrates are used as receptors by many viruses. Nonetheless, the biophysical rules that govern receptor recognition have not been established. Reoviruses provide a well-characterized experimental model of viral pathogenesis. They are nonenveloped, icosahedral viruses that contain a 10-segment dsRNA genome. These pathogens latch on to host cells via their attachment protein, Σ1. The molecule has a modular organization with distinct head-and-tail morphology. Various regions of the protein mediate attachment to receptors on eukaryotic cells. Specific sequences in the N-terminal tail bind carbohydrate. On the other hand, the C-terminal head binds to JAM-A, a surface immunoglobulin-superfamily member found in tight junctions.

Objectives:  
The objective of this research effort is to determine the function of Σ1 length in reovirus attachment and cell entry by characterizing Σ1 deletion reovirus mutants.

Methods and Materials:  
Three viral mutants harboring Σ1 molecules of different lengths were made to that purpose using site-directed mutagenesis and plasmid-based reverse genetics: L1-T3DS1 (lacks 7 predicted N-terminal β-spiral repeats: residues 161-291), L2-T3DS1 (lacks 10 C-terminal heptad repeats: residues 83-155), and L3-T3DS1 (lacks 5 predicted N-terminal β-spiral repeats and 10 C-terminal heptad repeats: residues 83-246). Their growth was assessed by plaque assay.

Results:  
The RP (reovirus particle) to PFU (plaque-forming unit) ratios for L1 and L2 appear similar to the wild-type virus ratio. On the other hand, L3’s RP/PFU value is at least four times that of the wild-type virus.

Conclusions:  
There seems to be a critical Σ1 length that allows for optimum infectivity. Shortening Σ1 may increase the steric hindrance from the bulk of the virion, impairing the interaction between the head of Σ1 and its receptor, JAM-A. The experiment discussed above will be repeated to ensure statistical significance of data. Further mutant characterization is forthcoming.

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Mentor(s) and Departments:  
Terense S. Dermody, M.D., Division of Pediatric Infectious Diseases and the Department of Microbiology and Immunology

ELECTROPHYSIOLOGICAL CHARACTERIZATION OF KV8.2, CANDIDATE GENETIC MODIFIER, IN THE SCN2A Q54 EPILEPSY MODEL

Courtney M. Campbell  
Medical Scientist Training Program

Background/Problem:  
Voltage-gated sodium channel mutations cause several types of human epilepsy. A transgenic mouse model Scn2aQ54 has a strain-dependent phenotype of partial seizures originating in the hippocampus. Scn2a Q54 on a C57BL/6 genetic background have a less severe manifestation than on a SJL/J background. Genome-wide interval mapping showed two modifier loci. Kv8.2, candidate modifier gene in one locus, is an alpha-subunit that complexes with Kv2.1, a delayed rectifier channel. Kv8.2 comparison between the strains revealed divergent amino acid sequences at two locations prompting our hypothesis that differences in the function of this potassium channel subunit account for the genetic modifier effect.

Objectives:  
To evaluate the electrophysiological properties of Kv8.2-C57BL/6 and Kv8.2-SJL/J when transiently co-expressed with Kv2.1.
Methods and Materials:
CHO cells were transiently transfected with plasmid DNA using FuGENE6. Whole-cell currents were measured with the patch clamp technique 48 hours after transfection using step-wise activation and cumulative inactivation protocols. Differences were assessed statistically using ANOVA.

Results:
Compared to Kv2.1 expression alone, Kv2.1/Kv8.2 exhibited reduced current density and a hyperpolarized conductance-voltage relationship. Kv2.1 channel alone had less than 10% cumulative inactivation. Kv2.1/Kv8.2 channels exhibited a 40% cumulative inactivation of initial current amplitude. Whole-cell electrophysiological properties of the Kv2.1/Kv8.2-C57BL/6 were indistinguishable from Kv2.1/Kv8.2-SJL/J indicating that strain differences in Kv8.2 amino acid sequence did not produce overt functional effects.

Conclusions:
<p>The electrophysiological properties of Kv8.2 in C57BL/6 and SJL/J mice co-expressed with Kv2.1 are identical in vitro. The mechanism of Kv8.2 as a modifier of epilepsy may be through an in vivo functional alteration such as expression level or membrane trafficking.</p>

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Mentor(s) and Departments:
Alfred L. George, Jr, M.D., Department of Pharmacology, Division of Genetic Medicine, Department of Medicine, Vanderbilt University Medical Center.

Conclusions:
These findings indicate that Shh is expressed by PCs and Shh signaling is present in BGCs of the adult cerebellum. The TNC-creER;Smifl- line can be used as a reliable model to study the effects of a lack of Shh signaling on development, maturation, and adult function of BGCs. Further studies will help elucidate postnatal roles of PC and BGC interaction and Shh signaling in BGCs.

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Mentor(s) and Departments:
Chin Chang, Ph.D., Cell and Developmental Biology Department, Vanderbilt University School of Medicine

LRP6 TRANSDUCES A CANONICAL WNT SIGNAL INDEPENDENTLY OF AXIN DEGRADATION

Christopher Cselenyi
Medical Scientist Training Program

Background/Problem:
Wnt/beta-catenin signaling controls various cell fates in metazoan development and is misregulated in several cancers and developmental disorders. Binding of a Wnt ligand to its transmembrane coreceptors inhibits phosphorylation and degradation of the transcriptional coactivator beta-catenin, which then translocates to the nucleus to regulate target gene expression.

Objectives:
To understand how Wnt signaling prevents beta-catenin degradation, we focused on the Wnt coreceptor low-density lipoprotein receptor-related protein 6 (LRP6), which is required for signal transduction and is sufficient to activate Wnt signaling when overexpressed. LRP6 has been proposed to stabilize beta-catenin by stimulating degradation of Axin, a scaffold protein required for beta-catenin degradation. In certain systems, however, Wnt-mediated Axin turnover is not detected until after beta-catenin has been stabilized. Thus, LRP6 may also signal through a mechanism distinct from Axin degradation.

Methods and Materials:
To establish a biochemically tractable system to test this hypothesis, we expressed and purified the LRP6 intracellular domain from bacteria and show that it promotes beta-catenin stabilization and Axin degradation in Xenopus egg extract.

Conclusions:
Using an Axin mutant that does not degrade in response to LRP6, we demonstrate that LRP6 can stabilize beta-catenin in the absence of Axin turnover. Through experiments in egg extract and reconstitution with purified proteins, we identify a mechanism whereby LRP6 stabilizes beta-catenin independently of Axin degradation by directly inhibiting GSK3’s phosphorylation of beta-catenin.

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COMPARATIVE MODELING OF hERG AND KCNQ1 WITH DRUGS CAUSING LONG QT SYNDROME

Elizabeth Dong
Medical Scientist Training Program

Background/Problem:
Voltage-gated potassium channels hERG and KCNQ1 are key in the repolarization of the cardiac action potential. Several drugs are known to bind these channels, causing cardiac arrhythmias such as long QT syndrome. Structural studies of these channels would enable the screening of drugs at risk of causing LQTS before their release to clinical trials. Computational structure prediction methods provide an opportunity to determine the interaction between drugs and these channels.

Objectives:
To build homology models and dock drug molecules to hERG and KCNQ1 to understand the structural determinants for drug-protein interactions.

Methods and Materials:
A Monte Carlo algorithm was used to determine optimized weight sets for bcl::align, a multiple sequence alignment tool that uses a customizable scoring function for sequence alignment. The methods of bcl::align will be redesigned to incorporate neural networks, increasing the speed and accuracy of alignments. bcl::align will be refined for membrane proteins, then used with hERG and KCNQ1 to determine a template for homology modeling. Using Rosetta, drug molecules will be docked to these comparative models.

Results:
In an evaluation of sequence alignment performance, bcl::align ranked best in alignment accuracy when compared with Align-m, ClustalW, T-Coffee, and MUSCLE. ROC curve analysis indicates bcl::align’s ability to correctly recognize protein folds with over 80% accuracy.

Conclusions:
The flexibility and accuracy of bcl::align allows it to be optimized for use with potassium channels involved in LQTS. Continuing research seeks to determine the interactions between hERG and KCNQ1 with molecules that hold therapeutic implications and elucidate the mechanism of such interactions.

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Mentor(s) and Departments:
Jens Meiler, Ph.D., Department of Chemistry and Center for Structural Biology, Vanderbilt University School of Medicine

A MOUSE MODEL OF HUMAN METAPNEUMOVIRUS INFECTION

John J. Erickson
Medical Scientist Training Program

Background/Problem:
Human metapneumovirus (hMPV) is a recently identified paramyxovirus that causes serious lower respiratory tract infection in children and immunocompromised individuals worldwide. Currently no vaccine nor therapeutic exists to prevent or treat infection. Mechanisms of immunity and pathogenesis have yet to be elucidated.

Objectives:
A critical first step towards understanding this important pathogen is establishing a mouse model of human infection.

Methods and Materials:
C57BL/6 (B6) mice were infected intranasally (106pfu/ml) in groups with one of four hMPV strains – A1, A2, B1 or B2. At 4 or 7 days post-infection, the mice were euthanized and their lungs and nasal turbinates were collected in order to titer viral loads.

Results:
Group A1, B1 and B2 viruses did not replicate in lungs or nasal turbinates to titers over 103pfu/gram. In contrast, hMPV-A2 replicated to 1.7±0.5x104pfu/gram in the lungs and 1.7±0.3x104pfu/gram in the nasal turbinates. Thus, subsequent work was focused on the A2 virus. A time course infection with hMPV-A2 demonstrated that lung and nasal viral titers peaked on day 5 (7.3±2.0x104pfu/gram and 5.1±1.8x104pfu/gram, respectively) and by day 7 began to decline. Histopathological examination revealed peribronchial and perivascular infiltration with CD3+ mononuclear cells.

Conclusions:
hMPV-A2 infection of B6 mice led to high titers of viral replication in both the lungs and nasal turbinates, with histopathological confirmation of host immune response. These findings indicate that the B6 mouse should serve as an accurate and appropriate model of human infection in which to conduct future experiments to elucidate the host immune response to hMPV infection.

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Mentor(s) and Departments:
John V. Williams, M.D., Division of Pediatric Infectious Diseases and Department of Microbiology and Immunology, Vanderbilt University School of Medicine

TUMOR SUPPRESSOR EFFECT OF SMAD4 EXPRESSION IN COLON CANCER

Tanner Freeman
Medical Scientist Training Program

Background/Problem:
Epithelial to mesenchymal transition (EMT) has been described in the progression of colon carcinoma (CRC). The Adenomatous Polyposis Coli (APC) protein is considered a gate-keeper of carcinogenesis in CRC. Smad4 functions as the central mediator in TGF-β signaling, and

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Mentor(s) and Departments:
John V. Williams, M.D., Division of Pediatric Infectious Diseases and Department of Microbiology and Immunology, Vanderbilt University School of Medicine
mutations in Smad4, implicated in 20-30% of CRC, are associated with later stages of EMT. The mechanism of Smad4 maintaining an epithelial phenotype without functional APC is unknown.

**Objectives:**
Elucidate a mechanism by which Smad4 expression induces an epithelial phenotype in transformed CRC cells.

**Methods and Materials:**
APC mutant, Smad4-expressing SW480 colon cells were engineered with a pCMV script expression vector (SW480Smad4/ SW480controls). Immunodetection for E-cadherin, β-catenin and vimentin was performed. Matrigel invasion assays were conducted comparing SW480controlsand SW480Smad4 while controlling for proliferation. Bilateral flank injections were administered by injecting SW480controls and SW480Smad4 into nude mice (n=16). Tumors were harvested 28 days after injection, and tumor volume was determined ex vivo.

**Results:**
E-cadherin co-localized with β-catenin to the cell membrane in SW480<sup>Smad4</sup> by immuno-fluorescence. E-cadherin was diffusely localized to the cytoplasm of the more spindly SW480 controls and β-catenin was both cytoplasmic and nuclear. Immunoblot showed vimentin to be down-regulated in SW480 Smad4 versus SW480 controls. SW480 Smad4 is significantly less invasive through matrigel than SW480 controls (p<0.001). SW480 Smad4 is significantly less tumorigenic in flank injections than SW480 controls (p<0.03).

**Conclusions:**
Smad4 loss in APC-mutated SW480 cells promotes EMT as evidenced by mislocalization of E-cadherin and β-catenin. Furthermore, Smad4 expression in SW480 cells is associated with reduced vimentin levels, in vitro invasion, and in vivo tumorigenesis.

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**Mentor(s) and Departments:**
R. Daniel Beauchamp, M.D. Department of Surgery, Vanderbilt University School of Medicine

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**MTBP IS A NOVEL REGULATOR OF MYC-INDUCED PROLIFERATION AND LYMPHOMA GENESIS**

**Brian Grieb**
*Medical Scientist Training Program*

**Background/Problem:**
Early reports suggest Mdm2 Binding Protein (MTBP) acts as a tumor suppressor by modulating Mdm2 and consequently p53; however, recent genetic data challenge this finding.

**Objectives:**
To examine the physiological function of MTBP and to determine its contribution to oncogene-driven B cell lymphomagenesis.

**Methods and Materials:**
Eu-myc transgenic mice, which overexpress the oncoprotein c-Myc in B cells and subsequently develop B cell lymphoma, were crossed with MTBP-deficient mice (MTBP<sup>+/−</sup>). Lymphomagenesis in MTBP<sup>+/−</sup>-Eu-myc and MTBP<sup>+/+</sup>-Eu-myc transgenic mice was evaluated. Proliferation and apoptosis were also examined in B cells from these mice.

**Results:**
Lymphomagenesis was significantly delayed in MTBP<sup>+/−</sup>-Eu-myc transgenic mice. Unlike Mdm2<sup>+/−</sup>-Eu-myc transgenic mice that have delayed lymphomagenesis due to increased p53-dependent B cell apoptosis, MTBP-deficient Eu-myc mice did not have an increase in B cell apoptosis. Instead, MTBP haploinsufficiency stunted Myc-driven proliferation, but did not affect Myc-induced apoptosis. An MTBP-deficiency inhibited the expression of Myc transcriptional targets that are important for proliferation. Moreover, MTBP expression was increased by factors that promote cell cycle progression. Lastly, MTBP mRNA and protein were overexpressed in both murine and human B cell lymphomas.

**Conclusions:**
The data suggest MTBP functions independently of Mdm2. Instead, MTBP may have oncogenic properties as a novel regulator of Myc-induced proliferation and tumorigenesis. Thus, MTBP warrants further investigation since Myc is overexpressed in up to 70% of human cancers and has thus far proven to be an evasive drug target.

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**Mentor(s) and Departments:**
Christine M. Eischen, Ph.D., Department of Pathology, Vanderbilt University School of Medicine

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**EFFECT OF CITED1 PHOSPHORYLATION ON NUCLEAR LOCALIZATION**

**Julia J. Kutaka**
*Medical Scientist Training Program*

**Background/Problem:**
CITED1 is a transcriptional cofactor, whose function is unknown, expressed in many different tissues during development. In the developing liver and kidney, CITED1 is localized to the cytoplasm. Nuclear localization of CITED1 is observed in the developing heart and Wilms’ tumor. This pattern of expression suggests that the nuclear localization of CITED1 may play a role in cardiac development as well as the pathogenesis of Wilms’ tumor. A recent study has shown that phosphorylation of CITED1 results in a mobility shift observed on western blot. We hypothesize that CITED1 phosphorylation affects nuclear localization.

**Objectives:**
To determine if nuclear localization of CITED1 is associated with its phosphorylation.

**Methods and Materials:**
We will isolate embryos at different developmental stages from E13.5 to E19.5. The localization of CITED1 will be studied in the kidney, heart, and liver, using immunofluorescence. A western blot of the protein lysates, with and without phosphatase treatment, will be carried out to look for a mobility shift. We will then identify the phosphorylation sites using mass spectrometry.
Results:
Consistent with previous data, CITED1 was localized in the nucleus of the developing heart. A mobility shift of CITED1, with the appearance of an additional high molecular weight band, was observed in lysates of E13.5 heart tissues. Treatment of lysate with phosphatase led to the loss of this additional band.

Conclusions:
These findings suggest that CITED1 gets phosphorylated in the developing heart. Further studies will be done to identify the phosphorylation sites using mass spectrometry, and to study the role of phosphorylation in the developing heart.

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Mentor(s) and Departments:
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INVASION OF THE CNS BY REOVIRUS

Caroline Lai
Medical Scientist Training Program

Background/Problem:
Many viruses cause central nervous system (CNS) infections, but little is known about mechanisms used by viruses to invade the brain. Endothelial cells adhere to each other via tight junctions, which contribute to the blood brain barrier. Several viruses utilize tight junction proteins as receptors. Reovirus is a tractable experimental model to study viral entry into the CNS. Junctional adhesion molecule-A (JAM-A), a tight junction protein, is a receptor for reovirus and promotes hematogenous dissemination of the virus to the brain. In addition to JAM-A, cell-surface sialic acid is a co-receptor for reovirus.

Objectives:
To determine the mechanism by which reovirus enters the CNS.

Methods and Materials:
A human brain endothelial cell line, TX-111, was infected with either of two reovirus strains differing in the capacity to bind sialic acid (T3SA+ and T3SA-). Infection was scored by immunofluorescence after 24 hours incubation. TX-111 cells were also treated with neuraminidase or antibodies specific to JAM-A (J10.4) prior to infection with T3SA+ and T3SA- viruses. Growth of T3SA+ and T3SA- was quantified at 0, 24, and 48 hours post-infection by plaque assay.

Results:
We found that TX-111 cells are susceptible to infection by T3SA+ and T3SA- reoviruses. The other experiments are in progress, and the results are pending.

Conclusions:
Since TX-111 cells are susceptible to reovirus infection, these cells will be a useful system to explore how reovirus infects endothelial cells. Future studies will establish the mechanism by which reovirus infects endothelial cells and disseminates to the CNS.

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Mentor(s) and Departments:
Terence S. Dermody, M.D., Division of Pediatric Infectious Diseases and the Department of Microbiology and Immunology, Vanderbilt University School of Medicine
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 causes 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 trilling the clinical question at hand, answer it with a feeling that it demands the best that it is in you, and when done look it over with a critical eye, not sparing a strict judgement 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.”
PLASMA TRYPTOPHAN & INCREASED RISK OF TRANSITIONING TO DELIRIUM AMONG ICU PATIENTS

Jessica R. Adams
Patient-Oriented Research

Background/Problem:
Serotonin, dopamine, and norepinephrine have been implicated in delirium pathogenesis. Their synthesis depends upon precursor bioavailability, reflected by plasma ratios of tryptophan (Trp), tyrosine (Tyr), and phenylalanine (Phe) to other large neutral amino acids (LNAA), respectively. Trp can alternatively undergo metabolism through the kynurenine (Kyn) pathway, in which the rate limiting step includes the production of kynurenine (Kyn) via indoleamine-2,3-dioxygenase (IDO; induced by inflammatory/immune responses) and may lead to neurotoxic effects.

Objectives:
This study aimed to determine if there was any association between: 1. The plasma ratios Trp/LNAA, Tyr/LNAA, and Phe/LNAA with increased risk of transitioning to delirium and/or 2. Plasma Kyn concentration and Kyn/Trp ratio (IDO activity) with poor neurologic outcome, thus decreased probability of delirium/coma-free days (DCFDs).

Methods and Materials:
Mechanically ventilated (MV) ICU patients enrolled in MENDS (JAMA, 2007) were evaluated for delirium via the Confusion Assessment Method (CAM-ICU). Aim 1 included: 97 patients, amino acid samples from days 1 & 3, analysis via liquid chromatography, 3 independent variables: Trp/LNAA, Tyr/LNAA, and Phe/LNAA, dependent variable: cognitive status (normal or delirium), and Markov regression modeling (associations between plasma LNAA ratios and risk of delirium transition). Aim 2 included: 85 patients, baseline plasma samples assayed similarly plus tandem mass spectrometry, 2 independent variables: Kyn concentration and Kyn/Trp ratio, and logistic regression analysis (associations between these and probability of DCFDs). Covariates for statistical analysis included: age, sedative exposure, and illness severity (APACHE II).

Results:
High and very low plasma Trp/LNAA ratios were independently associated with increased risk of delirium transition (p<0.0001), while ratios for Phe and Tyr were not. Baseline plasma Kyn concentration (p=0.01) and Kyn/Trp ratio (p=0.001) significantly decreased the probability of more DCFDs.

Conclusions:
In this study, plasma Trp/LNAA ratios, baseline Kyn, and baseline Kyn/Trp (IDO activity) were associated with increased probability of poor outcome (delirium transition risk or fewer DCFDs). This is the first study to analyze plasma Kyn pathway activity among MV ICU patients to examine its association with delirium.

Acknowledgements:

Mentor(s) and Department:
Pratik Pandharipande, M.D., M.S.C.I., Department of Anesthesiology, Division of Critical Care Medicine, Vanderbilt University Medical Center

BEHAVIORAL MEASURE OF REWARD FOR RESTRICTED INTERESTS IN AUTISM SPECTRUM DISORDER

Scott Bolton
Patient-Oriented Research

Background/Problem:
Autism spectrum disorders (ASD) are complex, behaviorally-defined developmental disorders that involve dysfunction in three domains: social relatedness, communication, and restricted or repetitive behavior. The third domain may manifest as a tendency for intense, circumscribed interests which can interfere with daily life.

Objectives:
To quantify the reward value of images related to these restricted interests by allowing participants to control the display duration of images either related or unrelated to their interest.

Methods and Materials:
Children and adolescents with ASD were compared to a matched control group with strong interests. Each participant viewed 60 randomized images that were either related or unrelated to their interests. The display duration was manipulated by the participant with unique buttons to either increase or decrease display time of each image.

Results:
The ASD group’s button presses resulted in longer display times for their own interests compared to controls’ presses for their own interests. There was no significant group difference in display time for unrelated images.

Conclusions:
Individuals with autism will often work and make extreme efforts to gain access to objects, activities, or media related to their restricted interests to the detriment of other behaviors. We found differences in the average amount of time that each group would view their respective interests. Expansion of this behavioral study using fMRI is currently underway in our laboratory.

Mentor(s) and Department:
Carissa Cascio, Ph.D., Department of Psychiatry, Psychiatric Neuroimaging Program, Vanderbilt University School of Medicine

SAFETY AND EFFICACY OF MINIMALLY INVASIVE MITRAL VALVE SURGERY WITHOUT AORTIC CROSS-CLAMP

Zachary E. Brewer
Patient-Oriented Research

Background/Problem:
Minimally invasive procedures are becoming a trend in many surgical fields with the goal of reducing patient morbidity and mortality. Traditional open heart surgery requires a sternotomy as well as aortic cross-clamping to provide a bloodless field, and can result in various postoperative complications including stroke, TIA, and sternal wound infection.

Objectives:
Assess the effectiveness and safety of performing minimally invasive heart surgery without aortic cross-clamping, specifically with a right anterolateral thoracotomy.

Methods and Materials:
The patient population for this retrospective study consisted of all patients who underwent mitral valve surgery through a right anterolateral thoracotomy.
Conclusion:

This procedure is safe with low complication and mortality rates, and provides excellent cosmetic results. Limitations to this method include that it is more technically challenging and requires a learning curve and initially possibly longer cardiopulmonary bypass times.

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Mentor(s) and Department:

John G. Byrne, M.D., Department of Cardiac Surgery, Vanderbilt University Medical Center

OBJECTIVE AND SUBJECTIVE COMPARISON OF 3T AND 7T MRI OF THE BRAIN

Aditi Desai
Patient-Oriented Research

Background/Problem:

Ultra high field (7T) MRI offers higher resolution images with enhanced signal-to-noise ratios (SNR), contrast-to-noise ratios (CNR), and image quality that may enhance detection of neuropathologies, yet not much literature exists comparing 7T MRI to clinical field strengths (3T).

Objectives:

To compare 7T and 3T MRIs of the brains of the same patients to objectively and subjectively assess the strengths and limitations of 7T MRI.

Methods and Materials:

Twenty-two patients undergoing clinical 3T scans were consented for a 7T scan. Image volumes of 3 comparable sequences at each field strength were graded by two neuroradiologists for anatomic visualizations, gray/white matter differentiation, image uniformity, and artifact severity. Three healthy volunteers were consented for duplicate scans at 3T and 7T to calculate SNR of caudate, putamen, and thalamus, and CNR of frontal, parietal, and occipital lobe gray/white matter at 3 comparable sequences at each field strength.

Results:

Table 1: Comparison of SNR and CNR at 3T and 7T

<table>
<thead>
<tr>
<th>Anatomical Region</th>
<th>SNR at 3T (%)</th>
<th>SNR at 7T (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudate</td>
<td>1.2</td>
<td>1.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Putamen</td>
<td>1.4</td>
<td>1.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Thalamus</td>
<td>1.3</td>
<td>1.6</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Conclusions:

Preliminary objective analysis of 7T versus 3T MRI demonstrates improved SNR of putamen and thalamus, and improved CNR of various cortical gray/white matter areas at multiple sequences, suggesting improved image resolution and quality. Subjective analysis pending.

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Jeff Creasy, M.D., Department of Radiology, and the Vanderbilt University Institute of Imaging Science

Mentor(s) and Department:

Jeff Creasy, M.D., Department of Radiology, Vanderbilt University School of Medicine

LINGUISTIC DEFICITS IN PATIENTS WITH EARLY PARKINSON’S DISEASE RECEIVING DEEP BRAIN STIMULATION

Lara L. Hershcovitch
Patient-Oriented Research

Background/Problem:

Parkinson’s Disease (PD) has been associated with impaired verb generation, with areas of the brain responding distinctly to different types of linguistic structure. One approach to studying this finding has been the Declarative/Procedural (DP) Model, where declarative memory supports the metal lexicon and the procedural memory supports grammar and rule-based items.

Objectives:

To assess the DP Model in early PD patients receiving Deep Brain Stimulation (DBS).

Methods and Materials:

Twenty-two PD patients already enrolled in a pilot trial, “Safety and Tolerability of Deep Brain Stimulation in Early Stage Parkinson’s Disease” were tested both while ON medication/DBS and after a 6-day washout period when they were OFF medication/DBS. Half of the patients received DBS and optimal drug therapy and the other half only received optimal drug therapy, but no DBS. In the Object Naming task, subjects are shown an object on the computer screen, either a non-manipulable object (i.e. an animal) or a manipulable object (i.e. a tool) and instructed to name it aloud. This task makes the assumption that subjects who have difficulty in their procedural memory will have a deficit in recognizing objects whose use rely on procedural memory (i.e. the physical action of using a wrench). The Past-Tense Production task tests regular and irregular verbs to compare a highly-predictable rule-like process (e.g. walk_walked) with an unpredictable idiosyncratic process (e.g. dig_dug). Subjects are shown a verb stem on a computer screen and instructed to inflect it aloud.

Results:

Data was analyzed using mixed effects linear modeling. There were no significant differences between subject groups, for either verb type, in either session, but group differences were seen between control and DBS subjects after a 6-day wash out period. For Object Naming, these differences are driven by slowed reaction times for manipulable items in the DBS group during session 2 (OFF-treatment). For Past-Tense Production, the difference between controls and DBS subjects in regular verb generation was observed, where reaction times for regular verbs in the DBS group during session 2 were faster. PD patients who had been receiving only optimal drug therapy performed like the controls in both tasks.
Conclusions:
While this study did not demonstrate a clear dissociation between impaired verb generation in a patient population with impaired procedural memory as seen in the DP Model, it did suggest a link between DBS treatment and language production. The DBS group performed particularly poorly on manipulable items while OFF medication/DBS, exhibiting the effects of impaired recall due to a deficit in items that rely on procedural memory. Results in the Past-Tense Production task suggested a general pattern of improved performance on regular verbs when this same group of patients was taken OFF DBS/medication. One possibility is that the subthalamic nucleus, which is functionally inactivated by DBS, may play a role in object naming and verb generation through non-motor basal ganglia thalamocortical circuits, by which it influences cognitive function.

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Mentor(s) and Department:
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DEEP BRAIN STIMULATION: ITS EFFECT ON RATE OF INCREASE OF ANTIPARKINSONIAN MEDICATION
Elyne Kahn
Patient-Oriented Research

Background/Problem:
Primate data suggest that subthalamic nucleus deep brain stimulation (STN-DBS) may slow disease progression in Parkinson’s Disease (PD). The effect has not been studied in humans due to ethical implications of withholding treatment from advanced PD patients. Change in anti-PD medication reflects disease progression in the absence of direct measurement.

Objectives:
The purpose of this study was to compare rates of increase of anti-PD medication between patients who receive STN-DBS versus medication-only patients.

Methods and Materials:
Clinic records were queried for patients with PD who had received bilateral STN-DBS (DBS arm). Ten subjects were randomly selected and PD patients who had not received DBS (MED arm) were matched by age at first anti-PD therapy. Levodopa Equivalent Daily Dose (LEDD) at each clinic visit was calculated using previously published equivalency formulas. Rate of increase was compared between groups using a mixed-effects model. To help achieve normality for the outcomes, we modeled LEDD after square root transformation. To improve accuracy of the results, we used the Kenward-Roger’s adjusted degrees of freedom solution for statistical inference (Kenward and Roger, 1997), an approach specifically proposed for small sample settings. With the estimated trajectories for each patient, we then compared the within-patient rates of progressions before and after surgery for each group separately, using the Wilcoxon Signed-Rank tests.

Results:
Before DBS, the rate of increase in LEDD was similar in MED and DBS subjects (p=0.7979), and at the time of DBS, patients in each group were receiving a comparable total LEDD (772 mg for the MED group and 961 mg for the DBS group). Following surgery, the rate of increase in LEDD again was not significantly different between the groups (p=0.3822). However, a significant difference was observed when comparing rate of increase in the DBS group before and after surgery (p=0.0001). This difference was not observed in the MED group when comparing rate of increase before and after the time at which their matched subject received surgery.

Conclusions:
We found that the there is a highly significant difference between the rate of increase of anti-PD medication before and after surgery in subjects receiving DBS. This result supports the concept of a potential neuroprotective effect of STN-DBS. This result is complicated, however, by the finding that there is not a significant difference in the rate of increase of medications between the DBS and MED subjects after surgery. An analysis of a larger sample may have demonstrated a significant difference. The result of a similar rate of increase in medication before surgery, and a comparable total LEDD at the time of surgery, supports the notion that the patients in both groups demonstrated a similar disease trajectory prior to receiving DBS.

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Mentor(s) and Department:
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INTRAOPERATIVE BLOOD LOSS PREDICTS HEMORRHAGE-RELATED REOPERATION AFTER ORHTOTOPIC LIVER TRANSPLANTATION
Stephen Kappa
Patient-Oriented Research

Background/Problem:
Previous studies have shown intraoperative transfusion requirement is the main determinant of reoperative intervention after orthotopic liver transplantation (OLT). We hypothesize that a transfusion requirement is a surrogate marker of intraoperative blood loss (IBL) in OLT.

Objectives:
The goal of this study is to develop an intraoperative hemorrhage model predicting reoperation after OLT.

Methods and Materials:
A single institution, retrospective review of adult primary OLT patients from January 2002 to 2008 was conducted. Multivariate logistical regression was performed using reoperation for postoperative hemorrhage as the response variable and IBL, pRBC and clotting factor transfusions, MELD score, cold and warm ischemia times, and operation duration as predictors. Secondary univariate analysis was conducted on patients in the reoperative group managed with temporary open abdomen techniques.

Results:
Four hundred ten primary transplantations were performed with 59 patients (14%) requiring reoperation. Multivariate analysis suggests the adjusted odds of reoperation when increasing IBL from 1.5 L to 10.0 L is 2.50 (95% CI: (1.18, 5.31)) with an adjusted IBL of 10.0 L predicting a
19% probability of reoperation. No significant associations were found for intraoperative transfusions or any other predictors. Reoperation patients managed with open abdomen (n=8) exhibited a significant IBL difference (16.0 L versus 6.0 L, p<0.001) when compared to the closed abdomen cohort.

**Conclusions:**
Intraoperative blood loss is the primary predictor of reoperation after OLT. A hemorrhage threshold of 10.0 L IBL predicts reoperation with a 19% probability. Secondary analysis suggests that IBL may also serve as a predictor for planned management with open abdomen, warranting further studies of this cohort.

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**Mentor(s) and Department:**
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**FUNCTIONAL MRI ASSESSMENT OF BASAL GANGLIA-THALAMOCORTICAL CIRCUIT ACTIVATION WITH MDMA USE**

John Karageorgiou

**Patient-Oriented Research**

**Background/Problem:**
MDMA (3,4-methylenedioxymethamphetamine) is a drug that produces long-lasting serotonin (5-HT) neurotoxicity consisting of reductions in markers for 5-HT axons. 5-HT innervates cortical and sub-cortical brain regions mediating motor function, predicting that MDMA users will have altered motor system neurophysiology.

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

**Methods and Materials:**
24 subjects (14 MDMA users, 10 controls) performed a motor tapping task (1, 2, 4 taps) during fMRI at 3T. Motor regions of interest were used to measure percent signal change (PSC) and percent activated voxels (PAV) in bilateral motor cortex, sensory cortex, supplementary motor area (SMA), caudate, putamen, pallidium and thalamus. We used SPM 5 to measure brain activation via three methods: T-maps, PSC and PAV.

**Results:**
There was no difference in reaction time between the two groups. For the Tap 4 condition, MDMA users had more activation than controls in the right SMA for T-score (p=0.02), PSC (p=0.04) and PAV (p=0.03). Lifetime episodes of MDMA use were positively correlated with PSC for the Tap 4 condition on the right for putamen and pallidum, with PAV in the right motor and sensory cortex and bilateral thalamus.

**Conclusions:**
In conclusion, we found a group difference in the right SMA and positive dose-response association between lifetime exposure to MDMA and signal magnitude and extent in several brain regions. 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.
SITAGLIPTIN’S EFFECT ON BLOOD PRESSURE RESPONSE TO ACE INHIBITION IN METABOLIC SYNDROME

Siri Kunchakarra
Patient-Oriented Research

Background/Problem:
Use of angiotensin converting enzyme (ACE) inhibitors, along with new oral hypoglycemic agents such as sitagliptin, a dipeptidyl peptidase-IV (DPP-IV) inhibitor, is rising due to increasing diabetes and hypertension rates. ACE inhibitors reduce blood pressure (BP) by decreasing degradation and potentiating the action of bradykinin and substance P, potent vasodilators. In the presence of ACE inhibitor, DPP-IV degrades substance P. We hypothesize that by inhibiting DPP-IV, sitagliptin will potentiate the BP lowering effect of ACE inhibitor via substance P.

Objectives:
To determine if the DPP-IV inhibitor sitagliptin potentiates the blood pressure response to acute ACE inhibition in the metabolic syndrome.

Methods and Materials:
We designed a prospective, randomized, double-blinded, placebo controlled parallel group cross-over study. Participants were randomized to group 1 (receive ACE inhibitor on both study days) or group 2 (receive placebo on both study days). Within each group, subjects were further randomized to receive sitagliptin prior to one study day and placebo prior to the other. BP is the primary endpoint, measured every five minutes on study days.

Results:
DPP-IV activity and ACE activity levels for completed subjects indicate we achieved our study design. Baseline glucose measurements were lower in subjects (n=20) on sitagliptin vs. placebo, consistent with known effects of sitagliptin on glycemia (100.8±2.0 vs. 96.4±1.5, p=0.03). By repeated measures ANOVA, sitagliptin causes a decrease in systolic BP (SBP) compared to placebo in normotensive subjects (n=5) on ACE inhibitor (p=.048).

Conclusions:
These preliminary data indicate that DPP-IV inhibition lowers SBP compared to placebo in normotensive subjects on ACE inhibitor.

Mentor(s) and Department:
Annis Marney, M.D., Loretta Byrne, R.N., and Nancy Brown, M.D., Department of Medicine, Vanderbilt University School of Medicine

SENSORY OUTCOMES AFTER SURGERY FOR INTERMITTENT EXOTROPIA

William McSwain
Patient-Oriented Research

Background/Problem:
Fusional testing in the management of intermittent exotropia remains controversial.

Objectives:
We report our experience with fusional status at near measured by the Stereo-Fly Test (Stereo Optical Co., Chicago, IL) before and after eye muscle surgery for intermittent exotropia.

Methods and Materials:
Retrospective case series. Sixty-seven children underwent bilateral lateral rectus recession and had motor outcome within 8 prism diptors of orthophoria at the 2-month postoperative visit. Vision, stereoaucity, and alignment were measured before surgery and at the 2-month postoperative visit.

Results:
Twenty-five children had non-detectable stereopsis preoperatively; six of these had detectable post-op stereopsis, but only one reached moderate grade (140 arc seconds). Forty-two children had low (200 arc seconds) to high grade (60 arc seconds or better) stereopsis preoperatively. Nineteen of these had no change in stereopsis after surgery. Ten children including five with poor initial (20 arc seconds) stereopsis developed 60 arc seconds or better. Of thirteen children with decreased stereopsis, eight
lost only one stereo circle. However, five children with initial moderate to high grade stereopsis had substantial loss; four of these had persistent small angle esodeviations, while all children who maintained or improved stereopsis had orthophoria or esodeviations postoperatively.

Conclusions:
Strabismus surgery can be associated with an improvement in near stereopsis in some children. Children with monofixational stereopsis prior to surgery have a higher incidence of significant stereo change. A persistent small angle esotropia at the 2-month postoperative visit is highly correlated with a loss of stereopsis. The loss of stereopsis in these children suggests that prisms or reoperation may be necessary to prevent this complication.

Mentor(s) and Department:
David Morrison M.D., Departments of Ophthalomology and Pediatrics, Vanderbilt University Medical Center

HEAD/NECK CANCER SURVIVORSHIP: FEASIBILITY OF EARLY PHYSICAL THERAPY FOR PHYSICAL/FUNCTIONAL RECOVERY

Audrey Metz
Patient-Oriented Research

Background/Problem:
Treatment for head and neck cancers (HNC) can be disabling with survivors frequently reporting functional deficits and a decline in health-related quality of life (HRQOL). These are associated with low survival rates suggesting an important yet unmet need for early intervention. The purpose of this pilot study is to determine the feasibility of an early physical therapy (PT) intervention targeting the physical needs of HNC survivors during combined chemotherapy and radiation (CCR) treatment.

Objectives:
The specific aims of this study are 1. Describe HNC survivors’ physical and functional HRQOL; 2. Describe HNC survivors’ range of motion (ROM) for the neck and shoulder and 3. Determine the feasibility of an early PT intervention over the course of CCR.

Methods and Materials:
This prospective, longitudinal study uses a convenience sample of HNC survivors at VUMC who are candidates for a standard course of CCR. Demographic, HRQOL, fatigue, social support and ROM data were collected at baseline, mid-completion of CCR, and two weeks post-CCR using reliable and valid survey and clinical tools (eg: FACT-G, PROMIS-fatigue, SSM, goniometer). Attendance to PT (the ratio of visits completed versus scheduled) was calculated to represent feasibility.

Results:
Twenty-three participants are enrolled and data collection is ongoing. The average age of participants is 55, 78% are male, 9% are African American, and 52% are married. On average, participants have 15 years of education and 47% report household incomes less than $40k per year.

Conclusions:
This study will provide information for the early identification and management of HNC-related physical and functional impairments before, during and after active treatment.

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Mentor(s) and Department:
Ann Marie Flores, P.T., Ph.D., M.S., M.A., Orthopaedics and Rehabilitation Institute, Vanderbilt University Medical Center

EXOSTOSES OF THE EXTERNAL AUDITORY CANAL IN WHITE WATER KAYAKERS

Ryan Moore
Patient-Oriented Research

Background/Problem:
Exostoses of the external auditory canal are benign tumors of the temporal bone associated with frequent cold water exposure. Obstruction may lead to conductive hearing loss and recurrent otitis externa, requiring surgery when symptoms become intolerable. Earplugs are recommended as protection but have never been associated with decreased prevalence.

Objectives:
To characterize the prevalence of exostoses in white water kayakers and identify significantly associated risk factors and protective habits.

Methods and Materials:
Six-hundred eleven white water kayakers were included in the study (median age 30, range 7-68; from 9 kayaking festivals across the US in 2008). Percent occlusion (determined by video ostoscope) was graded as normal (<25%), minimal (<25% with discrete exostosis), mild (25-50%), moderate (50-75%), or severe (>75%). Subjects completed a survey of risk factors and protective habits. Kruskal Wallis and Chi-Squared tests were performed to determine significant associations with percent occlusion.

Results:
The prevalence of exostoses in kayakers was 79% (482/611) – 30% (183/611) had ≥50% occlusion. Percent occlusion was associated with total years kayaked (p<0.001), frequency ≥ 1 day/week (p<0.001), male gender (p<0.001), age (p=0.005), and kayaking in the Pacific Northwest (p=0.018). Styles that involve repeated submersion were also associated (“freestyle” p=0.036; “squirt” p=0.016). Those using earplugs showed greater frequency of exostoses (p=0.007). However, those using earplugs for a greater proportion of their kayaking career were less likely to have exostoses (p=0.001).

Conclusions:
Kayakers are the first inland population to experience exostoses at the rates seen in surfers, divers, and other coastal populations. When used long-term, earplugs may be protective.

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Mentor(s) and Department:
Robert Labadie, M.D., Ph.D., Department of Otolaryngology, Vanderbilt University Medical Center
EVALUATION OF NEONATAL OUTCOME AND COST-EFFECTIVENESS ACHIEVED FROM OFFERING 24/7 FETAL FIBRONECTIN TESTING

Amulya Nagar
Patient-Oriented Research

Background/Problem:
Preterm birth is the leading cause of neonatal mortality and is a source of major economic burden to the health care system. Infants surviving past one year may suffer numerous short-term and long-term morbidities. Fetal fibronectin (fFN) testing in cervicovaginal fluid can help clinicians determine those women who will deliver preterm and will benefit from appropriate treatment with tocolytics or corticosteroids to improve fetal outcome. A negative fFN assay result in a woman with preterm labor symptoms predicts (>99% NPV) that there is minimal risk for delivery within 7 or 14 days of testing. This can be used by the clinician to avoid unnecessary treatments and hospitalizations.

Objectives:
To examine the benefits of increasing fFN assay availability at Vanderbilt University Medical Center (VUMC) from 8 hours/day, 5 days/week to 24 hours/day, 7 days/week on neonatal outcome and cost savings.

Methods and Materials:
This was a retrospective cohort study that included women presenting at the VUMC emergency department or obstetric clinics with the diagnosis of preterm labor over a two year period (one year before and one year after fFN testing became available 24/7). Pregnancy outcomes that were assessed included birth outcome (preterm or term), maternal morbidity due to adverse reactions to tocolytics and/or corticosteroids, fetal mortality, neonatal mortality, and neonatal morbidity due to preterm birth. Cost measures were related to admissions, tocolytic and/or corticosteroid prescriptions, and length of maternal and newborn hospitalizations.

Results:
Data collection is currently underway and progressing.

Conclusions:
Data collection is currently underway and progressing.

Mentor(s) and Department:
Alison Woodworth, Ph.D, Assistant Professor of Pathology, Vanderbilt University School of Medicine

POSTOPERATIVE NEPHROPATHY RISK FACTORS IN PATIENTS UNDERGOING CABG AND INTRAOPERATIVE GRAFT ANGIOGRAPHY

Ravneet Nagi
Patient-Oriented Research

Background/Problem:
Intraoperative graft completion angiography is an important tool for quality control after coronary artery bypass surgery (CABG). Since it is done intraoperatively, the surgeon can perform immediate revisions if defects are detected. An important point of discussion is the risk of adverse reactions to tocolytics or corticosteroids, fetal mortality, neonatal mortality, and neonatal morbidity due to preterm birth.

Objectives:
To quantify the risk of postoperative ARF and its further course in patients undergoing both CABG and intraoperative angiography.

Methods and Materials:
This is a retrospective study covering the period from March 2004 - July 2007. During this period 364 patients underwent CABG with routine intraoperative coronary angiogram. Preoperative, postoperative, and intraoperative data was collected from the Vanderbilt University Medical Center electronic database. ARF was defined as doubling of serum creatinine in 96h after surgery. Multiple logistic regression analysis was used to identify independent risks factors for nephropathy.

Results:
ARF occurred in 18/364 patients (4.9%). None required postoperative dialysis. Patients with ARF had higher incidence of preoperative acute myocardial infarction (28% vs. 13%, p=0.079), preoperative unstable angina (78% vs. 54%, p=0.055) and open chest (17% vs. 1%, p=0.001). Multivariate analysis showed that open chest (OR 37, 95% CI 4.8-289, p=0.001) was independently associated with ARF.

Conclusions:
Routine completion angiogram is safe. Patients with preoperative myocardial infarction and unstable angina are at increased risk of ARF. Open chest is the only independent predictor of ARF. No correlation was found between the amount of contrast agent used and the nephropathy rate.

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Mentor(s) and Department:
John G. Byrne, M.D., Department of Cardiac Surgery, Vanderbilt University Medical Center

THE EFFECT OF TIME ON RELATIONAL MEMORY

Jae Yoon Park
Patient-Oriented Research

Background/Problem:
Relational memory is the ability to learn associations between items. One form of relational memory is transitive inference (TI), i.e., the ability to infer relationships between items (e.g., A>C), based on prior learning of premise-pairs (A>B, B>C). Previously, Ellenbogen et al. (2007) demonstrated that TI performance improved after a significant time interval following training of premise-pairs.

Objectives:
The purposes of this study are to: 1. Further examine the effect of time by testing for relational memory performance at different time intervals following learning and 2. Identify possible relationships between learning style and relational memory.

Methods and Materials:
One hundred eight participants (subdivided into three groups) were trained on five premise-pairs (A>B, B>C, C>D, D>E, and E>F). Following a delay of 20 minutes, 6 hours, or 12 hours, participants were tested on their TI ability (B>D, C>E, and B>E). IQ and learning styles were assessed with questionnaires.

Results:
Participants in the three groups achieved similar levels of premise-pair proficiency during training (>90% accuracy) and retained similar levels of premise-pair knowledge after delay (>84% accuracy). In contrast to our
hypothosis, the three groups did not differ in their ability to make relational inference judgments (>63% accuracy, p=0.35). Different learning styles did not predict training or testing performance.

Conclusions:
In contrast to Ellenbogen et al., we did not find a significant effect of time on TI performance. Even after a short delay of 20 minutes, all three groups achieved accuracy significantly above chance during TI testing. We will conduct further analysis to determine what predicts TI after various time intervals.

Acknowledgements:
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Mentor(s) and Department:
Stephan H. Heckers, M.D., Department of Psychiatry, Vanderbilt University School of Medicine

CLINICAL OUTCOMES OF SINGLE VENTRICLE PALLIATION WITH PERSISTENT COMPETITIVE PULMONARY BLOOD FLOW
Alon Peltz
Patient-Oriented Research

Background/Problem:
Infants born without two normally functioning ventricles require a complex series of operations, called Single Ventricle Palliations, designed to allow the one functional ventricle to deliver oxygenated blood to the body and allow passive blood flow to the lungs. This study focused on post-operative recovery from an early part of this palliation, the Bidirectional Glenn Anastamosis (BDG). The BDG directs venous blood flow from the head and upper body to the lungs by connecting the Superior Vena Cava (SVC) to the pulmonary arteries. At the time of the BDG, the surgical team determines whether to leave the SVC as the lone source of pulmonary blood flow or to establish or maintain an additional source of pulmonary blood flow (APBF).

Objectives:
Determine if patients who underwent BDG with the additional sources of pulmonary blood flow (APBF +) had better post-operative outcomes when compared to patients who did not have an additional source of pulmonary blood flow (APBF -).

Methods and Materials:
We retrospectively evaluated the medical records of 125 patients who underwent BDG and pre-BDG catheterization at Vanderbilt Children’s Hospital between May 2001 – May 2008.

Results:
The results demonstrated that patients in this study with APBF were not at decreased risk for post-BDG complications and mortality (p=0.86) when compared to those without APBF. Clinical failure of the Glenn shunt was however found to occur at a higher frequency (p=0.001), in the APBF (+) group when compared with the APBF (-) group.

Conclusions:
Our results suggest that patients in this study who received BDG with APBF (+) were at higher risk for developing clinical failure of the Glenn shunt and did not demonstrate reduced post operative complications, improved long term oxygen saturation levels, or increased pulmonary artery growth when compared to patients without APBF (APBF -).

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RETURN TO PLAY FOLLOWING ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION IN FOOTBALL PLAYERS
Kevin D. Phelps
Patient-Oriented Research

Background/Problem:
The majority of outcomes associated with anterior cruciate ligament (ACL) injuries have been discussed previously. However, return to play following ACL reconstruction (ACLR) in an individual sport such as football has not been studied.

Objectives:
To determine the percentage of eligible football players from the Multicenter Orthopaedic Outcomes Network (MOON) database that returned to play following ACLR and to identify predictive factors.

Methods and Materials:
All MOON ACLRs from the 2002 cohort that listed football as either their primary sport, secondary sport, or sport of injury comprised the patient population. A unique questionnaire was designed, implemented, and administered over the phone to determine whether each athlete was able to return to play football following ACLR and, if not, whether factors previously undocumented in the MOON database (such as position played, competition level, time of injury, graduation, physician advice, or knee problems involving pain, swelling, instability, or fear of reinjury) were predictors of return to play.

Results:
Of 429 patients in the database, 119 (28%) listed football as a sport, of which 101 were eligible for follow up. For the first 6 months of the database, 24 of 34 eligible football players (70.6%) have been successfully followed up. For the last 6 months, 4 of the possible 63 (6.3%) have been followed up. Data collection continues in order to contact the remainder of the cohort.

Conclusions:
To increase the statistical power of the study, I will gather and include data from the 2003 MOON cohort before data analysis will be complete.

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Mentor(s) and Department:
Kurt P. Spindler, M.D., Vanderbilt Sports Medicine, Department of Orthopaedics and Rehabilitation, Vanderbilt University Medical Center
**Routine Completion Coronary Angiography and the Rate of Perioperative MI**

Jacob Elliott Schaff  
*Patient-Oriented Research*

**Background/Problem:**  
A serious complication of coronary artery bypass surgery (CABG) is graft failure. When this occurs intraoperatively, it can contribute to perioperative myocardial infarction (MI). Intraoperative coronary angiography is the “gold standard” for assessment of graft patency; if a defect is found, it can be repaired immediately without having to return to the operating room.

**Objectives:**  
The aim of this project was to see if routine completion coronary angiography decreases the rate of perioperative MI and improves clinical outcome.

**Methods and Materials:**  
This was a retrospective study between April 2005 and April 2006. During this period 199 patients underwent CABG followed by intraoperative routine completion angiogram and 126 patients underwent standard CABG with no confirmational imaging.

**Results:**  
Among the 438 imaged grafts, 61 (14%) angiographic defects were detected. Defects were repaired with either a minor adjustment of the graft (n=20, 4.5%) or with intraoperative percutaneous intervention or surgical revision (n=41, 9.5%). In comparison with patients who underwent standard CABG, those who underwent CABG followed by angiogram had no difference in rate of perioperative MI (1% vs. 2%, p=0.652) and in-hospital mortality (2% vs. 3%, p=0.710).

**Conclusions:**  
Routine completion angiography detected 14% of grafts with significant angiographic defects. No differences were found in the rate of symptomatic perioperative MI. However, “silent ischemia” in patients with occluded grafts was not taken into the account. It expected that follow-up routine completion angiogram performed at 12-18 months after surgery will make a difference in graft patency rate.

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John Byrne, M.D., Department of Cardiac Surgery, Vanderbilt University Medical Center

**No Association of Vaccines and Hyperammonemic Events in Children with Urea Cycle Disorders**

Cameron Schlegel  
*Patient-Oriented Research*

**Background/Problem:**  
Despite the success of childhood immunizations in the prevention of infectious diseases, questions remain about the safety of vaccines in children with inborn errors of metabolism, such as urea cycle disorders (UCD). Patients with UCD are a vulnerable population, subject to hyperammonemic episodes after infection, fever, or other stressors.

**Objectives:**  
We sought to assess the risk of hyperammonemic episodes resulting in subsequent hospitalization following routine vaccinations of pediatric patients with underlying UCD.

**Methods and Materials:**  
This was a retrospective epidemiological investigation of the impact of vaccinations on children with UCD within the longitudinal NIH sponsored Rare Disease Clinical Research Consortium for UCD. Vaccination records and hospitalizations due to hyperammonemic episodes were collected within the consortium with a molecular diagnosis of UCD. Each child’s post-vaccine exposure period was defined as 21 days following any immunization; the timing of hyperammonemic episodes with respect to vaccine exposure was investigated.

**Results:**  
The study enrolled 90 children under 18 years of age. The total number of immunizations was 1628, with an average of 21 ± 8.24 (S.D) vaccines per child. Hyperammonemic attack rates, during the 21-day post-vaccination exposure period and non-exposure periods were 8.0% and 6.2% per patient-month of observation, respectively (Fisher Exact p=0.14). The rate ratio in the post-vaccine exposure vs. non-exposure periods was 1.3 (95% confidence interval: 0.9, 1.8).

**Conclusions:**  
No association between hyperammonemic episodes and vaccinations was suggested by our preliminary analysis in children with UCD. Further analysis of this data set using different time intervals will be performed to ensure the safety of immunization in this vulnerable population of high risk children with UCD.

**Acknowledgements:**  
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Mentor(s) and Department:  
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**Mtdna Depletion Complicating Cardiopulmonary Bypass in Children Having Cardiac Anomalies Surgically Repaired**

Brittni H. Schoonover  
*Patient-Oriented Research*

**Background/Problem:**  
Nearly 1% of live births are complicated by the presence of a congenital cardiovascular defect, which are surgically repaired with the aid of cardiopulmonary bypass. Mitochondrial DNA deletions have been observed in adult populations undergoing CABG; however, the association between cardiopulmonary bypass and mitochondrial toxicity in children is unknown.

**Objectives:**  
To assess the effects of cardiopulmonary bypass on mitochondrial DNA copy number.

**Methods and Materials:**  
Blood samples were collected from 30 children undergoing surgical repair of congenital heart defects. Blood was collected at the following times: before bypass was initiated, at 30 minutes on bypass, following cessation
of bypass, 2 hours post bypass, and 6 hours post-bypass. Total genomic DNA was purified using the DNeasy Blood and Tissue Kit (Qiagen). Real-time PCR was used to determine mtDNA copy number using TaqMan assays (Applied Biosystems) with probes specific to mitochondrial gene ND5 normalized to the nuclear gene for RNaseP.

Results:
Mitochondrial DNA copy number declined progressively across all study time points (p<0.01), with the largest decline (46.3%) occurring between the pump30 and post-pump time points (p<0.001). We observed that the acyanotic physiologic subgroup had a significantly larger decline in mtDNA than the group with cyanotic physiology (p<0.01).

Conclusions:
Cardiopulmonary bypass in children undergoing surgical correction of congenital heart anomalies leads to a significant decline in mtDNA. Loss is most drastic during bypass administration, which cannot be fully explained by loss of platelets as previously observed. Further studies will look at more intensive markers and cell subsets.

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Mentor(s) and Department:
Jeffrey A. Canter, M.D., M.P.H., Center for Human Genetics Research, Vanderbilt University School of Medicine

NON-OPERATIVE TREATMENT OF PARTIAL ACL TEARS

Michelle Shepard
Patient-Oriented Research

Background/Problem:
While complete tears of the anterior cruciate ligament (ACL) have been well studied, few studies have investigated the natural history of and optimal treatment for partial ACL tears.

Objectives:
To characterize the natural history of partial ACL tears in a highly active population.

Methods and Materials:
From 2002–2007, patients with a partial ACL tear identified at surgery were deemed candidates for non-operative treatment if they had 1. a solid endpoint on Lachman, 2. less than full pivot shift, and 3. 50% of ACL fibers intact in normal anatomic configuration on arthroscopic examination. Thirty-six patients meeting these criteria were contacted to determine if they had progressed to a complete ACL tear requiring reconstruction and were mailed validated outcomes questionnaires to assess changes in knee function and activity level.

Results:
Of the 36 patients with a partial ACL tear, 33 (92%) were contacted at an average of 42 months (median 37, SD 21) from presentation. Only 2 of 33 patients (6%; 95% CI, 2% – 20%) required ACL reconstruction. The average Marx activity score within the partial tear cohort dropped 2.09 points between the time of surgery and follow-up, as compared to 4 points among patients with complete tears who underwent ACL reconstruction.

Conclusions:
Short-term results suggest that there may be a subgroup of patients with partial ACL tears that do not require reconstruction. The proportion requiring subsequent ACL reconstruction is similar to that of revision surgery for primary ACL reconstruction. The rate of progression is similar to the incidence of ACL tears in the general population.

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Mentor(s) and Department:
Kurt P. Spindler, M.D., Department of Orthopaedic Surgery, Vanderbilt University Medical Center

SHORT TO MID-TERM RESULTS OF A NEW UNCEMENTED ENDOPROSTHETIC STEM

Robert Wilson
Patient-Oriented Research

Background/Problem:
Limb salvage surgery with an uncemented endoprosthesis is an emerging treatment strategy for bone lesions. Currently most endoprostheses are cemented into bone, but have continued to have high failure rates.

Objectives:
The purpose of this study is to assess the short to mid-term clinical and functional outcomes for the uncemented press-fit Stryker® Global Modular Replacement System (GMRS) endoprosthesis.

Methods and Materials:
Between 2003 and 2007 35 patients required surgical implantation of the press-fit GMRS endoprostheses. The Toronto Extremity Salvage Score (TESS) survey and the Musculoskeletal Tumor Society 1987 (MSTS) survey were administered to assess functional and clinical outcomes. Radiographs were evaluated for evidence of aseptic loosening, fracture, infection, and local tumor recurrence. Kaplan-Meier analysis was used to evaluate implant survival.

Results:
Follow-up was obtained for all 35 patients with endpoints of either last clinic visit or death. The average age at surgery was 34 years. Twenty of the 35 patients were receiving chemotherapy in the perioperative period. The average follow-up was 37.9 months (range 6-71). Sixteen of 35 patients completed the MSTS and TESS surveys. The average MSTS score was 33 out of 35. The average TESS score was 74.78 out of 100. The Kaplan-Meier estimate of the overall survival rate of the prostheses for all patients was 85% at 60 months. There was one incidence of stem subsidence and 2 perioperative infections (stems retained).

Conclusions:
Short to mid-term functional and clinical outcomes for the uncemented press-fit GMRS endoprosthesis compare favorably with other cemented and uncemented endoprostheses. Long-term follow-up of the endoprosthesis is warranted.

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