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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 areas in which students can choose projects: Biomedical Informatics, Patient-Oriented Research, Laboratory-Based Biomedical Research, Healthcare Research and Management, Law, Community Health Initiatives and Health Outreach, International Health, Medical Humanities, and Education. 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 first and second year while being 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.

As well, students who are part of our Medical Scientist Training Program are 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 of the projects carried out by the Class of 2009, the second class to complete the Emphasis Program. The broad range of projects reflects the broad range 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 intervening summer. As Director of the Emphasis Program, I want to express my thanks to those who so 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 101 abstracts represent 13 oral presentations and 88 posters that were presented at the Emphasis Forum at Vanderbilt University from April 25th to 27th, 2007. Ninety of these abstracts represent the work of students who entered the Emphasis Program in the fall of 2005. Twelve 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 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 are to judge from the work presented herein, the overarching goal of nurturing scholarship and leadership in our students has already been successful.
Kevin Johnson, MD, is an Associate Professor and Vice Chair of Biomedical Informatics with a joint appointment in the Department of Pediatrics. He has been an active participant in the informatics efforts of many national organizations including the Institute of Medicine, the American Medical Informatics Association, the American Board of Pediatrics; the American Research in Healthcare Technologies. His research areas are electronic prescrip-
tion-writing systems development; the uses of advanced computer technologies, including the Worldwide Web, personal digital assis-
tants, and pen-based computers in medicine; and the development of computer-based documentation systems for the point of care.

"It has been very exciting to observe students as they learn about the field of biomedical informatics. One student, who was concerned about the impact of technology on learning, is in the midst of writing up some very intriguing results. We have also had students with significant technical backgrounds who have made landmark contributions to the field. The Emphasis program is allowing students to exchange knowledge among themselves, our faculty, and our graduate students, in a way that will sharpen the skills of all three groups."

Methods and Materials: To understand how registries function in clinical practice, we implemented the NSN as a prototype MDR in the Vanderbilt Orthopaedic Institute. The process, successes and failures of implementing the NSN registry were documented as a case study. To better understand registries other than NSN, we conducted a review of the scientific literature discussing MDRs.

Results: We collected articles discussing data-
base projects self-identified as "registry." We then constructed a set of over 40 registries, from which we extracted a list of all descriptive attrib-
utes. Finally, we grouped these attrib-
utes into a comprehensive set of six features that are fundamental to reg-
istry design and function. We used five of these characteristics as the basis of a registry definition and scor-
ing system, which we call the FLAPS score. A database must demonstrate all five characteristics—Follow-up, Longitudinal, Aggregable, Prospective, and Standardized—thus scoring five (5) in the FLAPS system, to meet our definition of a registry. The sixth characteristic (inclusion principle) is bivariate and we use this in our taxonomy to distinguish two varieties of registries.

Conclusions: Contrary to popular convention, we propose that the term “registry” is rigidly defined and its usage should be limited to a subset of medical databases. We have proposed the FLAPS scoring system to classify a database as a registry, and as a taxonomical system for all databases. Finally, our narrative experience of the NSN reg-
discusses pitfalls and suggestions for successful implementation of a prototype registry.
Background/Problem:
A DNA biobank is defined as a repository of genetic information correlated with patient medical records. DNA biobanks may assist in the research and identification of genetic factors influencing disease and drug interactions, but may raise ethical issues. How healthcare providers perceive DNA biobanks is unknown.

Objectives:
To determine how useful healthcare professionals believe DNA biobanks will be and whether these attitudes differ between private and socialized healthcare systems.

Methods and Materials:
The authors surveyed 200 healthcare professionals, including research and non-research focused doctors, nurses and other staff from medical centers and independent practice in both the United States and Scotland. The survey included fifteen items evaluating general receptiveness toward biobanks, presumed usefulness of biobanks, and perceived attitudes in recruiting patients for a biobank.

Results:
A total of 81 (45%) of 179 eligible participants responded: 41 from the United States and 40 from Scotland. Of these respondents, most (76%) were from academic centers. Results indicate that there is a broadly favorable attitude in both locations toward the creation of a DNA biobank (83%) and its perceived benefit (75%). This enthusiasm is tempered in Scotland when respondents were asked to evaluate their comfort in consenting patients for entry into a biobank: 16 of 40 respondents were uncomfortable doing so, representing a significant difference from those in the United States (p = 0.001).

Conclusions:
Despite systematic differences in healthcare practice between America and Scotland, health care professionals in both nations believe DNA biobanks will be useful in curing disease. This finding appears to support further development of such a research tool.

Acknowledgements:
S. Trent Rosenbloom, MD, MPH, Vanderbilt University Medical Center and Nancy Lorenzi, PhD, Vanderbilt University Medical Center; Jeremy Wyatt and Alex Doney, University of Dundee, Scotland, UK. Thank you to the Health Informatics Centre at the University of Dundee for facilitating my research. Thank you also to the Overall Fellowship for supporting the overseas aspects of my research.

Community Health Initiatives and Health Outreach

The Emphasis Program area of 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 underserved 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.

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.

“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.”
Empiric Treatment of Sudanese Lost Boys and Girls for Schistosomiasis and Strongyloidiasis

Jose Eduardo Alvarado
Community Health

Background/Problem: The Lost Boys and Girls of Sudan are a group of refugees living in the United States as a result of civil war that arose in their homeland and displaced them from their homes. The vast majority of these refugees were forced as children to walk hundreds of miles through East African jungles and rivers to reach safety. After arrival to the United States, many of these refugees complained of chronic stomach/GI pain. At the 2004 National Lost Boy/Girl Reunion in Arizona, the CDC conducted a study to assess the prevalence of schistosomiasis and strongyloidiasis in this population. The study showed prevalence rates of 44% for schistosomiasis and 49% for strongyloidiasis. Although both were highly suspected to be causing the chronic GI pain, the rates of symptoms were actually the same among both the infected and unaffected refugees. However, because of the long-term complications of these two infections and the relative ease and safety of treatment, the CDC recommended that all Lost Boys and Girls of Sudan be empirically treated for schistosomiasis and strongyloidiasis. Objectives:

1. To administer empiric treatment for schistosomiasis and strongyloidiasis to the Lost Boys and Girls of Sudan in the Nashville in the most cost-effective and culturally sensitive manner.

Methods and Materials: Recruitment of Lost Boys and Girls took place through three means: announcement of project at church services that are attended by a majority of the Lost Boys/Girls in the Nashville area; distribution and posting of an informational flyer; and word of mouth through the Lost Boys Association of Nashville. Treatment was administered through large scale treatment days at St. Bartholomew’s Episcopal Church and a future event to be held at Siloam Family Health Center. Treatment consisted of 20 mg/kg of praziquantel given in two oral doses 6 – 8 hours apart for schistosomiasis and 400mg of albendazole twice a day for 3 days for strongyloidiasis.

Results:
Three treatment dates were held and a total of 42 Lost Boys/Girls came for treatment. Two patients chose not to be treated because their exposure and risk factors were not high enough to justify empiric treatment. The other 40 patients were treated and administered the short survey. There were no major reported side effects from the treatment.

The short healthcare survey administered indicated that 23 of 40 (56%) Lost Boys who came for treatment currently had health insurance. This number was higher than expected in this population, but shows that a significant portion of these refugee’s are without insurance. The survey also indicated that the most effective recruiting methods were church announcements and word of mouth from friends.

Conclusions:
The empiric treatment of the Lost Boys/Girls of Sudan population has proved quite challenging from the standpoint of logistics. It was our hope at the onset of the project to treat over 100 of the estimated 200 Lost Boys living in the Nashville area. The main barrier was finding dates and locations that would result in high turnouts. Many of these Lost Boys work full time jobs in addition to being full time students which limits their time availability. Secondly, they have limited means of transportation due and are dependent on others for rides due to the poor public transportation in Nashville.

We will continue holding treatment dates in hopes of reaching more Lost Boys. Future treatment events will be planned to coordinate with already established community events to improve community access to care.

Acknowledgements:
Dr. Morgan Wills MD; Siloam Family Health Center, St. Bartholomew’s Episcopal Church of Nashville, TN; Schering-Plough Corporation.

Risk Factors for Childhood Obesity in the Nashville, Tennessee Hispanic Population

Roxs Coleman
Community Health

Background / Problem: Obesity is a major health problem in the United States and increases the risk of diabetes, coronary heart disease, and hypertension. The prevalence of obesity is greater among Hispanics, a rapidly growing population in Nashville, than the general population. Within this community local health clinics noted a rise in childhood obesity, which once established may become chronic.

Objectives:
The purpose of this study was to identify risk factors contributing to obesity among Hispanic children in Nashville and to determine maternal feeding practices, health knowledge and perceptions of healthy weight.

Methods and Materials:
Surveys were administered to 117 Hispanic mothers with children between 2 and 6 years at two outpatient clinics. The BMI was obtained on each child for whom the survey was completed. 40.6% of the children had a BMI above the 85th percentile (at-risk). 21.9% of the children were above the 95th percentile (overweight). 50% of mothers with at-risk children reported that a doctor had not discussed their child’s weight with them. Among at-risk children, 72.7% of their mothers were not worried about their child’s weight. Mothers of overweight children were significantly more likely to be worried about their child’s weight than mothers of children not over-weight. However, mothers of children at-risk were not more worried about their child’s weight when compared to mothers of children not at-risk. Overweight or at-risk children were less likely to have whole milk in the house. Analysis is ongoing.

Conclusions:
Obesity has not yet been drawn.

Addressing and Assessing the Amount of Daily Activity in a Transitional Living Community

Kate Groh
Community Health

Background:
Many people in this country experience barriers to daily exercise and activity. This is the case at the subsidized transitional living community, Mercy Court, in Nashville. Chronic diseases like obesity, diabetes, hypertension, and heart disease are prevalent in this community. Through their relationship with the Dayani Center and the Vanderbilt University School of Nursing, Mercy Court has benefited from free medical screenings and health assessments. We have taken this a step further by working with Nashville public housing to create a sustainable and effective program that may help improve their health and well-being.

Objectives:
1. To improve the health and well-being of the residents of Mercy Court by increasing daily activity levels, which will be assessed by self-reporting, as well as through comparison of individual’s weight, BMI, and body circumference at the beginning and end of the six week program.
2. To provide health education concerning issues of activity, fitness, and diet, as well as diseases such as diabetes, hypertension, and heart disease.
3. To help this group of people sustain a recommended amount of daily activity by using pedometers and keeping daily health logs.

Methods and Materials:
Participants were given a pedometer to measure their daily steps. They also attended weekly meetings for 6 weeks, where we discussed issues of health and disease. Half of the participants kept daily health logs, assessing variables like exercise, sleep, nutrition, and overall well-being. We also had a follow-up meeting to assess participants’ health status 4 months after ending the program.

Results:
All participants noted an increase in daily steps over the course of the 6 week program. Their increase in physical activity also coincided with a self-reported improvement in sleep, nutrition, and overall well-being. Participants also noted difficulty with maintaining an active lifestyle after the program ended, for various reasons. Health statistics such as BMI were collected approximately a month before starting the program, and will be compared with the data collected 6 months after completing the program.

Conclusions:
Pedometers appear to be an inexpensive and effective way to help people increase their activity level. They may become less effective as health-promoting tools over time, due to tendency to discontinue their use.
Shade Tree Family Clinic: More than Another Loop in the Safety Net

Caroline Knox
Community Health

Background/Problem: The Shade Tree Family Clinic (STFC) is a free health clinic run by Vanderbilt medical students. Directors have observed that STFC has been serving its target population of underinsured patients in East Nashville, but these observations have not been quantified.

Objective: Survey patients to gather information about why they came to STFC and to identify any barriers they have faced in getting health care.

Methods and Materials: Using an instrument I designed, I surveyed walk-in patients at STFC. From August to November 2006, I invited every English-speaking adult patient in the waiting room to participate.

Results: 75% of 57 patients surveyed were uninsured. When asked if “in the last three years have you ever needed health care and not gotten it?” 35% circled “Yes” with “lack of insurance” as the main reason. When asked “When you think about your health and medical needs not currently being met?” 20 patients reported having medical debt (mean $3,267). When asked “Why did you come to STFC instead of another clinic?” answers included “lack of copay,” “hours,” “location,” “recommended by a friend,” and “because I trust the people here.” When asked “How could we make this clinic better for you?” patients suggested shorter wait times, more space, longer hours, more medication options and the addition of a social worker.

Conclusions: STFC patients have complex medical and social needs. STFC is filling a much needed gap in health care services. Services for patients can be improved as STFC expands and further establishes itself within the safety net.

Acknowledgements: Dr. Robert Miller, Barbara Clinton, Barbie Chadwick, Americorps, the Tennessee National Health Service Corps S.E.A.R.C.H. Program, and the Arnold P. Gold Foundation.

Medical Students’ and Residents’ Knowledge and Experience of Complimentary Alternative Medicine

Brandon Litzner
Community Health

Background/Problem: The use of complementary and alternative medicine (CAM) has greatly increased over the past fifteen years, slowly integrating with traditional medicine. In this new integrative climate, physicians are required to be knowledgeable about the safety and efficacy of various alternative treatments. Multiple studies have tried to determine how much knowledge and experience practicing physicians have regarding CAM, but few have looked at medical students and residents.

Objectives: To evaluate the knowledge and experience of Vanderbilt University’s first and fourth year medical students and third year residents with respect to CAM.

Methods and Materials: A survey was developed and administered that assessed the knowledge, personal use, recommendations, and interest in learning of the medical students and residents with respect to sixteen different CAM modalities, including acupuncture and yoga. Demographics were also collected.

Results: One hundred and sixty surveys were completed – 55 first year medical students, 54 fourth year medical students, and 50 third year residents, which correspond to response rates of 52.9, 52.9, and 37.3%, respectively. Sixty-three percent (99) of the respondents were between 20 and 25 years of age, 54% (84) were male, and 73% (115) were white. The knowledge, personal use, recommendations, and interest in learning of all CAM modalities surveyed, aside from massage and vitamins, were less than 35% frequent in all training groups. Compared to the medical students, the third year residents were less interested in learning about any CAM modality.

Conclusions: The knowledge and experience of CAM of the physicians in training surveyed is limited and interest appears to decrease with training.

Complimentary and Alternative Medicine Education for HIV+ Individuals

John Pitts
Community Health

Background/Problem: The use of complementary and alternative medicine (CAM) by people living with HIV has been reported between 40 and 60%. However, many HIV+ CAM users do not report their CAM use to their doctors, which can be hazardous, and many may not be properly educated in the use of these alternative treatments. Lastly, many HIV+ individuals are simply unaware of the potential benefits of CAM.

Objectives: To generate educational tools that address the potential benefits and risks of using CAM for the Nashville CARES, middle Tennessee’s leading community-based AIDS service organization.

Methods and Materials: CAM modalities and their use, both in general and in HIV+ individuals, were comprehensively researched using literature reviews, internet searches, and interactions with CAM practitioners.

In turn, a holistic health brochure and a PowerPoint presentation were created. The brochure was distributed to all CARES clients, while the PowerPoint presentation was used by CARES in future educational workshops. An acupuncturist was also recruited to give a presentation on acupuncture and its use in HIV and addiction. A flyer advertising the PowerPoint and acupuncturist’s presentations were included in the mailing of the brochures.

Results: The brochure was mailed to over 2000 CARES clients. The PowerPoint presentation was not utilized during the time frame of the study. Two CARES clients and three staff members attended the acupuncturist’s presentation and provided positive feedback on the brochure and presentation.

Conclusions: While the brochure and advertisement of the presentations were able to reach a large audience, very few recipients attended the presentations.

Acknowledgements: Dr. Nancy Chescheir, my faculty mentor; Brandon Litzner, my research partner; Barbie Chadwick and Barbara Clinton, my community Health area heads; Dr. Beth Barnett, my community mentor; Ken Barton for his assistance at CARES; and Rhonda Cook for hosting the acupuncture presentation.

Assessing the HIV-Related Knowledge Attitude, Beliefs and Behaviors of MSA Nashville, Tennessee Youth

Jennifer Y. See
Community Health

Background: While the vast majority of Tennessee high school students report having been taught about HIV/AIDS in school, HIV and STD infections as well as risky sexual behavior among youth in Tennessee remain prevalent problems. It has been shown that standardized HIV education and prevention messages do not effect the same behavioral change in youth of diverse backgrounds. Therefore, in order to develop effective HIV education programs that target the local youth population, the youth’s HIV-related knowledge, attitudes, beliefs, and behaviors (KABB) must be investigated and better understood. The HIV-related KABB of the Metropolitan Statistical Area (MSA) Nashville youth population has not been studied.

Objectives: To assess the HIV-related KABB of the MSA Nashville youth population aged 13-18. To develop a survey protocol, survey administration training tools, and partnerships within the MSA Nashville community so that Nashville CARES, Middle Tennessee’s AIDS service organization, may perform this assessment on a periodic basis.
Methods:
This descriptive study was conducted at public venues where youth aged 13-18 are known to frequent, including youth-oriented events, community centers, water parks, skate parks, food establishments near schools, and bowling alleys. Participating youth were given a self-administered written questionnaire. Questions assessing knowledge of HIV transmission and prevention utilized an open-ended format. Questions on risk reduction likelihood, risk reduction self-efficacy, comfort discussing HIV/AIDS, and perceptions of HIV/AIDS as a reality utilized a 4-point Likert scale.

Results:
354 youth residing in MSA Nashville were surveyed. Nearly all youth (324; 91.5%) indicated sex as a way of transmitting HIV, but for bodily fluids that transmit HIV, only 102 (28.8%) indicated semen, 81 (22.9%) “sperm,” 50 (14.1%) vaginal fluids, and 32 (9.0%) “sexual fluids.” For methods of protection, 227 (64.1%) indicated abstinence, 317 (89.5%) indicated condoms or safe/protected sex, and the median level of self-efficacy for those respondents’ use of the respective identified methods was “very able” for both. On average, the youth had a moderate level of comfort discussing HIV-related issues with an adult and had a low level of concern that they might become infected with HIV or have contact with someone living with HIV.

Conclusions:
Youth HIV educators may need to place greater emphasis on how HIV is transmitted through sex via bodily fluids. Future studies should assess to what degree the youth’s low level of concern about becoming infected with HIV is because the youth feel they are able to protect themselves or because they feel their likelihood of coming into contact with someone living with HIV is low. Assessing the HIV-related KABB of the MSA Nashville youth population provides information that local youth HIV educators can use to design education programs targeting the unique needs and cultural backgrounds of the local youth. In addition, continuous assessments of the youth population’s HIV-related KABB will enable HIV educators to assess the effectiveness of their programs.

Acknowledgements:
Co-authors: Patrick W. Luther, MHS, Nashville CARES; Lynette Dufton, MS and Theresa Ulman, MS, Vanderbilt University; and Victoria Harris, EdD, Vanderbilt University School of Medicine. Funding provided by the Vanderbilt University School of Medicine Emphasis Program, the Arnold P. Gold Foundation, and the Tennessee Primary Care Association. Thank you to Barbara Clinton and Barbee Chadwick for community partnership advice and to Lisa Kaltenbach and Theresa Scott for statistical advice.

Healthcare and Public Health Research and Management

The student experience in the area of Healthcare and Public Health Research and Management is designed around two tracks:
1. Healthcare research and
2. Healthcare management.

The research track is focused on hypothesis-driven investigation in a field of healthcare research, which includes clinical epidemiology and outcomes 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.

Robert S. Dittus, MD, MPH is the Albert and Bernard Werthan Professor of Medicine and Chief of the Division of General Internal 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. His epidemiology, health services and policy research has improved the effectiveness, efficiency, timeliness, safety and equity of healthcare. 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.

“In the Healthcare 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.”

Acknowledgements:
Co-authors: Patrick W. Luther, MHS, Nashville CARES; Lynette Dufton, MS and Theresa Ulman, MS, Vanderbilt University; and Victoria Harris, EdD, Vanderbilt University School of Medicine. Funding provided by the Vanderbilt University School of Medicine Emphasis Program, the Arnold P. Gold Foundation, and the Tennessee Primary Care Association. Thank you to Barbara Clinton and Barbee Chadwick for community partnership advice and to Lisa Kaltenbach and Theresa Scott for statistical advice.
Background/Problem: If maternal depression is not treated, it presents a risk to both mother and fetus during the months of pregnancy. If the depression is treated with SSRIs it may still pose a threat to the fetus. In order for the true risk to the fetus to be estimated, however, there first needs to be an assessment of how frequently these drugs are prescribed to pregnant women.

Objectives: To assess the rate of change in the trends of prescribing antidepressants to women with pregnancy-related visits to physicians in the United States between the years of 1995 and 2005 and to identify groups of women at high risk for pregnancy exposures to antidepressants.

Methods and Materials: This was a study of trends using cross sectional data. Women with diagnoses related to pregnancy were identified using the NAMCS/NHAMCS data. Each time an antidepressant prescription was written for one of these women, it was recorded. Trends in prescribing of antidepressants to women with pregnancy-related visits were calculated.

Results: Results are summarized in the two tables below.

### Assessment of the Core Competencies of the Chief Medical Officer

<table>
<thead>
<tr>
<th>Competency</th>
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<tr>
<td>Healthcare</td>
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### Impact of Emergency Department Occupancy and Patient Boarding on Nurse Work Patterns

#### Catherine Dale

**Healthcare Research and Management**

**Background:** Emergency Departments (ED) are becoming overcrowded due to increased utilization and patient boarding. The impact of crowding and boarded patients on registered nurse (RN) workload has not been studied.

**Objective:** To describe the work patterns of ED RNs and compare patterns during periods of low and high occupancy and patient boarding. The study also examined the impact of increasing task demands on RNs' subjective assessments of workload and quality.

**Methods and Materials:** Using time and motion task analysis, a convenience sample of 16 RNs caring for non-trauma patients in a Level 1 Adult ED were studied. Each RN was observed twice for approximately 180 minutes, once in the morning and once in the afternoon, of the same shift. Surveys were administered every hour to assess each RN's subjective ratings of workload. Statistical analyses were performed using paired t-tests and linear regression.

**Results:** The core competencies of the CMO have changed in light of the move toward transparency in health care. Secondly, CMOs are not well prepared for many of the competencies identified as most important. Therefore, training and education for CMOs is necessary for preparing the physician executives for the "new age" CMO with particular emphasis on certain core competencies.

**Conclusions:** The core competencies of the CMO should be reassessed. Changes should be made in the way that RNs are trained and prepared for their expanding role in the ED. This study also examined the impact of increasing task demands on RNs' subjective assessments of workload and quality.

**Acknowledgements:** William O. Cooper, MD, MPH, and Theresa A. Scott, MS, Vanderbilt University Medical Center.

**Methods and Materials:** Eighteen naïve Vanderbilt University medical students completed 20 hours of colonoscopy training on the GI Mentor. Nine of 18 students were randomly assigned to receive coaching. Subjects sequentially practiced 10 scenarios. Six experienced endoscopists completed six of the same scenarios in a prescribed sequence over two hours. For each scenario, simulator software calculated performance metrics. Generalized linear mixed models analysis of variance were used to compare individual trainees’ performance with experienced endoscopists groups as well as trainer versus experienced participant groups.

**Results:** Intragroup variation was substantial. Thus, there were no significant differences between uncouched and coached groups’ peak performances or in the time required to reach proficiency. Trainees’ performances after two hours on a scenario were comparable to experienced subjects’ performance on the same scenario. Experts were initially faster and smoother yet saw less mucosa, but as cases progressed statistically significant differences disappeared. Both trainees and coaches demonstrated statistically significant learning over time. Coaches’ performance was superior to experienced endoscopists.

**Conclusions:** This study showed the overall benefit of procedural simulator training, but failed to find a significant effect of coaching in the training paradigm studied. Future studies should examine transfer of training to actual colonoscopies.

**Acknowledgements:** Dr. Matthew Weinger, Dan France, PhD, and Rebecca Dezube, Vanderbilt University Medical Center.

**Procedural Learning in Simulated Colonoscopy**

**Rebecca Dezube**

**Healthcare Research and Management**

**Background:** Colonoscopy simulator training may improve clinicians’ performance during patient procedures. There is little data on how best to implement procedural simulators into training curricula. In other domains, directed feedback back through coaching improves learning.

**Methods and Materials:** Using time and motion task analysis, a convenience sample of 16 RNs caring for non-trauma patients in a Level 1 Adult ED were studied. Each RN was observed twice for approximately 180 minutes, once in the morning and once in the afternoon, of the same shift. Surveys were administered every hour to assess each RN’s subjective ratings of workload. Statistical analyses were performed using paired t-tests and linear regression.

**Results:** The core competencies of the CMO have changed in light of the move toward transparency in health care. Secondly, CMOs are not well prepared for many of the competencies identified as most important. Therefore, training and education for CMOs is necessary for preparing the physician executives for the “new age” CMO with particular emphasis on certain core competencies.

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**Conclusions:** This study showed the overall benefit of procedural simulator training, but failed to find a significant effect of coaching in the training paradigm studied. Future studies should examine transfer of training to actual colonoscopies.

**Acknowledgements:** Dr. Matthew Weinger, Dan France, PhD, and Rebecca Dezube, Vanderbilt University Medical Center. And Dr. Caroline Cao, Tufts University.
Refractive Error After Spontaneously Regressed Retinopathy of Prematurity

Matthew E. Emanuel
Healthcare Research and Management

Background: Retinopathy of prematurity (ROP) is a potentially blinding disease of the eye. Even with spontaneously regressed disease, frequent examination is often performed to detect high refractive error, anisometropia and strabismus. However, there is a paucity of evidence-based guidelines that suggest appropriate follow-up intervals for these children.

Objectives: To review the development of anisometropia after a normal first examination in children with spontaneously regressed ROP.

Methods and Materials: Retrospective chart review. A normal cycloplegic refraction prior to 18 months of age. Children with a history of threshold ROP at the pediatric ophthalmologist with cycloplegic refraction was defined as ametropia after a normal first examination. A normal first examination in children with spontaneously regressed ROP.

Results: Six hundred sixty children were identified with a diagnosis of ROP. Of those, 428 were examined by a pediatric ophthalmologist with cycloplegic refraction prior to 18 months of age. Seven hundred sixty children were included. Two hundred twenty-three patients were discharged from the ICU and 43 patients died in the ICU. Among families of discharged patients, family attendance was associated with higher satisfaction regarding coordination of care (p=0.013). Though the total FS-ICU and decision-making subscale scores were higher among family members who attended family rounds, these differences were not significant.

Conclusions: Among specific dimensions of the ICU experience that were expected to be most affected by family rounds in this study, some significant increases in satisfaction were associated with family attendance.

Race Differences in Virologic Response to Antiretroviral Therapy

Bryan D. Harris
Healthcare Research and Management

Background/Problem: Previous reports have suggested that racial disparities exist in health outcomes among patients receiving antiretroviral therapy (ART). A pilot CQI investigation of patients on ART at the Comprehensive Care Center (CCC), a large outpatient HIV treatment center in Nashville, Tennessee, indicated that Blacks were less likely to achieve virologic suppression.

Objectives: To analyze the differences in virologic outcomes among racial subsets of patients followed at the CCC.

Methods and Materials: All patients seen from January through May, 2006 and any with an ART start date prior to January 1, 2006 were included in this study. Of the 1084 patients who met the criteria, 697 (64%) were Caucasian, 321 (30%) African-American, and 66 (6%) were classified as other. Patients were assigned to a response or failure group determined by their most recent HIV-1 RNA level (>50 copies/mL = failure).

Results: Univariate logistic regression analyses demonstrated that a number of factors were associated with failure. Black race, increased time in care, low CD4 count prior to current ART, mental health diagnoses, longer duration of therapy prior to current ART, higher number of previous ART regimens, lack of an NNRTI in current ART, non-MSM transmission risk and AIDS diagnosis. In a multivariable model, only low CD4 count prior to current ART, higher number of previous ART regimens, lack of an NNRTI in current ART, and non-MSM transmission risk were significantly associated with virologic failure.

Conclusions: The initial racial differences observed in virologic response among patients receiving ART at the CCC were no longer significant in a model which controlled for several associated variables.

Acknowledgments: To increase communication and EOL planning between family members and the medical team through daily "family rounds" in the ICU.

Family Rounds in the ICU: Improving Communication and End-of-Life Experiences in Critical Care

Natalie Jacobowski
Healthcare Research and Management

Background: Family members of ICU patients need extensive interaction and communication with the medical team due to the complexity of critical illness and related treatments. Over 30% of families do not understand ICU patients' diagnoses, prognosis, or treatments. We hypothesized that early and more frequent family/family-centered communication would improve family satisfaction with the ICU experience as well as specifically enhance end-of-life (EOL) planning.

Objectives: To examine communication and EOL planning between family members and the medical team through daily "family rounds in the ICU.

Methods and Materials: Families were invited to attend daily rounds in the medical ICU in which the interdisciplinary medical team discussed the care plan and other disease management issues. A lay summary directed to the family followed, with an opportunity for questions and family interaction with the team. Family satisfaction was assessed by the validated "Family Satisfaction in the ICU (FS-ICU)") survey, administered by phone (N=123) to family members of patients admitted to the ICU for greater than 24 hours over a six-month period spanning pre- and post-implementation of family rounds.

Results: Families representing 278 ICU patients participated; 227 patients were discharged from the ICU and 43 patients died in the ICU. Among families of discharged patients, family attendance was associated with higher satisfaction regarding coordination of care (p=0.013). Though the total FS-ICU and decision-making subscale scores were higher among family members who attended family rounds, these differences were not significant.

Conclusions: Among specific dimensions of the ICU experience that were expected to be most affected by family rounds in this study, some significant increases in satisfaction were associated with family attendance.

Observation of these increases in both the discharged and EOL families suggests benefits of such an intervention for all ICU patients. Family rounds attendance was not associated with an increase in overall family satisfaction as measured by the FS-ICU survey. Given the generally high scores from all respondents, the FS-ICU may not be sufficiently sensitive to detect a change in satisfaction. The significant increases in satisfaction with particular aspects of care suggest a need for future study of the potential impact of implementing a family rounds system.

Acknowledgments: E. Wesley Ely, MD, MPH, John Mulder, MD, Timothy Girard, MD, and John F. Fox, MD, Vanderbilt University Medical Center and Andrea Dugas, Vanderbilt University School of Medicine.

The Integrative Health Consult: A Collaborative Approach to Patient Care

Brennessa M. Lindeman
Healthcare Research and Management

Background: Studies have shown that many Americans use complementary and alternative modalities of care without knowledge of their primary care physician. Many of these interventions have been shown to provide benefit and should be incorporated into the current healthcare system.

Objective: To create a model for the Integrative Health Consult (IHC) that incorporates aspects of both conventional and complimentary therapies.

Methods and Materials: This descriptive study was conducted by literature review and analysis of the IHC process at other academic institutions. An ideal client flow process plus measures to assess quality of life were determined using psychometric analysis.
Results: The model of the IHC described was implemented at the Vanderbilt Center for Integrative Health on December 1, 2006. The model consists of a two-visit system in which clients will initially meet with a practitioner for relationship-building and data gathering. Measures of quality of life that will be assessed in all clients are: Readiness to Change scale, Quality of Life Index, Spiritual Perspective Scale, and CES-D Depression Questionnaire. The treatment team will then meet to discuss the practitioner’s initial plan for the client and the client will return to develop a Collaborative Health Plan with the practitioner, where health goals will be defined in concrete terms.

Conclusions: Integrative Health Consults are an effective way to understand an individual's history and current state of health. A Phillip visit system in which clients will initially meet with a practitioner for relationship-building and data gathering. Measures of quality of life that will be assessed in all clients are: Readiness to Change scale, Quality of Life Index, Spiritual Perspective Scale, and CES-D Depression Questionnaire. The treatment team will then meet to discuss the practitioner’s initial plan for the client and the client will return to develop a Collaborative Health Plan with the practitioner, where health goals will be defined in concrete terms.

Acknowledgements: Johnny Lu Healthcare Research and Management

Survey of Healthcare Professionals Regarding Management of Delirium and Sedation in the Intensive Care Unit

Rina Patel Healthcare Research and Management

Background: In the ICU, delirium can occur in up to 80% of mechanically-ventilated patients. Previous studies have shown that ICU delirium is associated with higher mortality and prolonged length of stay. Sedative use is one of the risk factors for delirium. Wes Ely, et al conducted a survey in 2001 regarding ICU delirium. The survey was informative, but was informally written and did not examine sedation behaviors.

Objectives: 1. To revise the 2001 survey to address any methodological weaknesses. 2. To determine changes in behaviors or attitudes regarding ICU delirium.

Methods and Materials: The survey was edited and validated with two pilot runs. The final survey includes 11 multiple choice and Likert scale items. The survey was administered to healthcare professionals at Vanderbilt University Medical Center.

Results: Analysis has only been conducted on surveys from HCA (140): 24% thought that delirium occurred in more than half of mechanically-ventilated ICU patients, 6% used a specific delirium scale, 48% used general clinical assessment, and 46% did not screen for delirium. Eighty-one percent used a sedation protocol.

Conclusions: Delirium in the ICU is not as well managed as sedation. Very few respondents used a delirium scale, as recommended by national guidelines. However, a majority of people used a sedation protocol. The results analyzed were limited to HCA hospitals and might be biased. More than 1200 surveys have been collected from other locations. This results will, hopefully, provide a better picture of national behaviors.

References:

Acknowledgements: E. Wesley Ely, MD, MPH, Vanderbilt University Medical Center.

Optimal Dose Categories for Use in Epidemiologic Studies of Nsaids and Coxibs

Vernon A. Rayford Healthcare Research and Management

Background: Problem: A substantial number (30-40%) of individuals who undergo chemotherapy treatment report mild cognitive declines that may persist for years. Common complaints associated with “chemo-brain” include difficulty multi-tasking (executive function), performing simple motor tasks, retrieving short-term memories (declarative memory) and remembering names (verbal memory). On the other hand, regular aerobic exercise is shown to have significant beneficial effects on many of the same kinds of cognitive function that are affected by “chemo-brain.” We are unaware of any studies looking at exercise and its effects on cognitive function in this clinical population.

Objectives: 1. To describe the association between fitness levels or amounts of lifetime exercise and levels of cognitive function that are affected by childhood versus adulthood exercise or vigorous versus moderate exercise and levels of cognitive function. 2. To determine any changes in behaviors or attitudes regarding ICU delirium.

Methods and Materials: The survey was edited and validated with two pilot runs. The final survey includes 11 multiple choice and Likert scale items. The survey was administered to healthcare professionals at Vanderbilt University Medical Center.

Results: Analysis has only been conducted on surveys from HCA (140): 24% thought that delirium occurred in more than half of mechanically-ventilated ICU patients, 6% used a specific delirium scale, 48% used general clinical assessment, and 46% did not screen for delirium. Eighty-one percent used a sedation protocol.

Conclusions: Delirium in the ICU is not as well managed as sedation. Very few respondents used a delirium scale, as recommended by national guidelines. However, a majority of people used a sedation protocol. The results analyzed were limited to HCA hospitals and might be biased. More than 1200 surveys have been collected from other locations. This results will, hopefully, provide a better picture of national behaviors.

References:

Acknowledgements: E. Wesley Ely, MD, MPH, Vanderbilt University Medical Center.
The objective of this study is to examine the attitudes of Vanderbilt University Medical Center’s first (PTM1) and fourth year medical students (PTM4) and third year residents (PITM3) toward IM, in order to appropriately guide future educational activities to better promote health and healing.

Methods and Materials:
The Integrated Medicine Attitudes Questionnaire (IMAQ), used to evaluate attitudes toward IM was administered, and expanded to include the statement: Medical schools should teach students about IM. Demographics were also collected.

Results:
Even though the proportion of PITs surveyed who agreed that medical schools should teach IM was significantly associated with gender (female PITs showing a higher proportion), race and PIT group were not significantly associated. In general less than half of the PITs surveyed agreed that medical schools should teach IM. Female PITs also reported more positive attitudes toward IM, demonstrated by statistically significant differences in responses to half the IMAQ attitude statements.

Conclusions:
The study results agree with current literature, overall a majority of PITs agree that IM should be taught as part of medical education and more female PITs desire to include IM in medical education and female PITs report more positive IM attitudes. The study found that an overall majority of PITs support medical education teaching IM; this highlights the discrepancy between the prevalence of IM use in the general population and current trends in medical education curricular reform integrating more IM themes, with the lack of support from PTs for IM.

References:

Acknowledgements:
Nancy Chesneir MD, Roy Elam, MD, Paul Keckley, PhD, Brandon Litmer, BS, John Pitts, BA, Theresa A. Scott, MS and Patti Thomas, BA, Vanderbilt University Medical Center.
International Health

The focus area of International Health provides students an opportunity to learn about issues of global health through participation in projects based in other countries. Potential projects encompass the full range of themes in international health, from medical sciences and clinical investigation, to socio-cultural correlates of health and health care delivery. Participation in an International Health elective and other directed study will provide background for work abroad.

Peter Wright, M.D., is Co-Principal Investigator for the Vanderbilt HIV Vaccine Program. Dr. Wright initiated HIV vaccine research at Vanderbilt in 1987, and has been directing HIV clinical trials since that time. Dr. Wright has a special interest in mucosal immunity to HIV. He has also worked closely with investigators at Cornell University and GHESKIO in Port-au-Prince, Haiti to bring HIV vaccine research to the Caribbean. Dr. Wright is Professor of Pediatrics and Microbiology and Chief of the Pediatric Infectious Diseases Division at Vanderbilt.

“International Health was a late addition to the initial year of the Emphasis program at the impetus of students with interests in this area. In the first year, four students participated in very diverse projects, all of which involved spending the summer between the first and second years in an international setting. The interest in the International Health Emphasis area has grown such that currently there are 16 first year students who have elected to have training abroad. This parallels a recognized trend and resurgence in interest in medical students in participation in International Health that was recently highlighted in a Perspective the New England Journal of Medicine.

The International Health emphasis area contributed to a broadening of expectations for students completing the Emphasis Program. The initial goal was for the student to produce a very defined product, specifically a paper prepared for a journal. In the Emphasis Program in International Health there has to date been a health clinic built in Kenya, a new prospective on women’s rights from Mali, an insight into the global polio eradication program in India and a description of an association of meliodiosis and the use of statin drugs from aborigines in Australia. For each student the experience has substantially changed their perspective on medicine and their future careers.”

Credit for the growth in the International Health area must be fully shared with our new Institute for Global Health headed by Dr. Sten Vermund whose enthusiasm and access to students through an office in Light Hall has greatly facilitated and refined the aspirations and expectations of students to match with the realities of work in the International Health arena.”

Review of Prevention of Mother-to-Child Transmission (PMTCT) Interventions in Pune, India

Neena Agarwal
International Health

Background: India has more people living with HIV/AIDS (5.7 million) than any single nation. With a birth rate of 25 million and a seroprevalence rate among pregnant women of ~0.9%, it is expected that in absence of a prevention of mother to child transmission (PMTCT) program, about 7500 HIV infected neonates will be born yearly. We studied the implementation of a PMTCT program attempting to respond to this challenge run by an NGO, ‘Prayas’ in Pune, Maharashtra.

Objectives: To qualitatively review the PMTCT implementation activities at three of Prayas’s program sites, with special focus on the unique needs of individual patient populations.

Methods and Materials: Prayas is implementing a PMTCT program in eight hospitals in and around Pune. We visited three of their program implantation sites serving different patient populations. The first site was visited on five separate occasions, site two on three separate occasions, and site three on two separate occasions. We observed and assisted in pre- and post-HIV test counseling activities, post-delivery care and follow-up. In addition, we conducted an in-depth interview with each counselor. An interview with a member of the program administration was also conducted to assess criterion used in choosing the counselors, training methods and data management of enrolled patients.

Results: The pre-counseling was done in groups. Women attending the clinics were counseled about their risk and the necessity of confidential HIV testing, as well as consequences and actions after a positive or negative HIV test result. The counseling was done with messages that were focused and tailored to the educational level of the patient. We observed that the counselors had excellent training and communication skills, but some of them often got overwhelmed with the work load. Prayas has a well-developed, intensive two-week training program for counselors. Advanced data management software was used for patient records; which was helpful in patient tracking and follow-up. The program staff was highly motivated and appropriately skilled and efficient.

Conclusions: The intervention is especially effective because it educates women about the dangers of the HIV and gives them the power with choices within the context of the cultural norms. Although there were limitations with privacy during counseling sessions, the program has many strengths including the sensitivity of the counselors, optimal use of available resources and effective data management. Although public sector programs for PMTCT in India often lack this dedicated, multifaceted approach, efforts are currently ongoing to replicate and scale-up the Prayas-run program in the public sector through public-private partnerships.

References: Available upon request.

Acknowledgements:
Co-authors: Megan Galloway, College of Arts and Sciences, Vanderbilt University and Vikrant V. Sahasrabuddhe, MBBS, MPH, DrPH, Vanderbilt University School of Medicine. I would like to thank Dr. Vikrant Sahasrabuddhe for his guidance and instruction throughout my research and Megan Galloway for her support over the summer. I am grateful to the members of the Prayas organization for their time and advice during my research. I would also like to thank the Vanderbilt School of Medicine Emphasis Program for the funding to make this work possible.

Expansion of HIV and Syphilis into the Peruvian Amazon: A Study of Four Chayahuita Communities

Ellika Bartlett
International Health

Background: The first known outbreak of HIV and syphilis in the Chayahuita indigenous group was discovered in 2004 (Am J Trop Med Hyg, 2007; in press), highlighting the need for further research into the prevalence and impact of HIV and syphilis in this population.

Objectives: To determine the prevalence of HIV and syphilis in four Chayahuita communities and to identify behaviors, practices, and beliefs that may increase the risk for infection.

Co-authors: Megan Galloway, College of Arts and Sciences, Vanderbilt University and Vikrant V. Sahasrabuddhe, MBBS, MPH, DrPH, Vanderbilt University School of Medicine.

References: Available upon request.
Methods and Materials: Consent was obtained from participants and blood samples were tested for HIV and syphilis infection. Quantitative and qualitative data were collected through a survey, focus groups and interviews, including demographic information, risk factors for STI transmission and knowledge and beliefs about HIV/AIDS.

Results: We collected 282 blood samples and conducted 282 interviews. The confirmed prevalence rate of syphilis was 9/282 (3.2%) and 5/135 (3.7%) for men and 4/147 (2.7%) for women. The prevalence rate of HIV infection was 2/282 (0.7%), with both infections in MSM. The prevalence of self-reported sex between men was 50/129 of sexually active men (38.7%). There was poor knowledge about HIV infection, transmission and prevention.

Conclusions: We confirmed the presence of HIV and syphilis in additional Chayahuita communities at rates equal to and higher than the national averages respectively. We also identified many communities at rates equal to and higher than the national averages respectively.

Elispot Quantization of MSP-1 Specific Memory B-Cells After Infection With P. falciparum
Karl Becak
International Health

Introduction: In contrast to areas of sub-Saharan Africa where malaria infection by P. falciparum parasite reaches epidemic proportions, in the Amazonian villages around Iquitos, Peru, incidence and transmission is low but stable. Research from the MIGIA (Malaria, Immunity and Genetics in the Amazon) project has shown that individuals of these communities possess a lasting titer of antibody directed against the MSP-1 (Merozoite Specific Antigen), a major immunogenic protein of the parasite, in individuals for at least one month post-infection.

Objective: To detect and quantify the presence of antigen-specific memory B-cells that may be responsible for the production of relatively long-lasting antibody titers to MSP-1 (QTSR) by developing a reliable ELISPOT assay on-site in the Amazon jungle.

Methods and Materials: Blood samples were collected from individuals of Peruvian Amazon communities one month after resolution of P. falciparum infection (cases) and from individuals of urban Iquitos who were never exposed to the parasite (controls). PBMCs were isolated by Ficoll gradient, counted and cultured +/- Pokeweed Mitogen and fixed S. pombi, and plates were analyzed on-site in the Amazon jungle. The development and dissemination of culturally appropriate pre-knowledge. The development and dissemination of culturally appropriate pre-knowledge. The development and dissemination of culturally appropriate pre-knowledge. The development and dissemination of culturally appropriate pre-knowledge. The development and dissemination of culturally appropriate pre-knowledge.

Adherence to Antiretroviral Therapy in Rural Zambia
Jimmy Carlucci
International Health

Background: Nearly 17% of Zambians are infected with HIV. As antiretroviral therapy (ART) becomes increasingly available, barriers to care must be assessed. Barriers to adherence are particularly important as levels of <95% are necessary for optimal clinical outcomes and to prevent emergence of antiretroviral drug-resistant strains of HIV.

Objective: To assess travel to point of HIV/AIDS care as a potential barrier to adherence in rural Zambia and to study the influence of demographics, BMI, WHO stage, and stigma.

Methods and Materials: This study included 424 patients receiving ART from the Macha Mission Hospital (MMH). Interviews revealed age, sex, education, perceived stigma, nearest rural health facility (RHF), mode and cost of transportation awaiting result of each patient. Motorcycle odometer and GPS way-points measured distance from the MMH to each of the RHFs. Distances were used as estimates of patients' home-to-MMH travel distance. BMI, WHO stage, pill counts and pharmacy records were extracted from patients' medical charts. Pill counts and pharmacy records were used to calculate adherence.

Results: We discovered that 83.7% of patients had >95% adherence to ART. Travel issues did not predict adherence. Total days over which adherence was measured for each patient ("total days") was highly associated with adherence (p<0.0001). Adherence across "total days" increased up to 80 days of observation after which time adherence started to decline.

Conclusions: We believe that complications and hardships faced during cell culture and ELISPOT in the Amazonian environment introduced significant error into our experiment. Error analysis is ongoing to determine the exact cause of our difficulties and how such problems can be avoided in the future.

Household Profiles and Needs Assessment for Orphans and Vulnerable Children in Natal, South Africa
Megan Carr
International Health

Background/Problem: South Africa is currently an epicenter for the global HIV epidemic. One outcome of the crisis has been a rise in orphans and vulnerable children (OVC). This study seeks to obtain empirical data on the status and needs of OVC in two communities of KwaZulu-Natal, South Africa. The OVC participating in this project are currently enrolled in a local intervention program designed by a local NGO.

Objectives: Assess the status and needs of OVC living in KwaZulu-Natal by creating a baseline and follow up database for a local NGO. Areas under investigation include demographics, education, household, health profile and psychosocial development. A secondary objective is to evaluate the efficacy of the NGO intervention over its three year lifespan and to develop a model that informs local and national OVC programs and policy.

Methods and Materials: This project involves the design, distribution and analysis of a 100-point interview questionnaire. Interviews are administered to the OVC and caregivers of the OVC at six month intervals between 9/2006-9/2009. To date, 78 OVC and 52 caregivers have participated and completed Phase I of the interviews (9/2006 and 2/2007 data collection points).

Results: This study is ongoing and I am currently analyzing the data from the February 2007 collection point. Without comparative data as of yet, the most meaningful results are from the demographic profile. On average, the OVC live in families of 6 +/- 2 people. Twenty-one percent of the OVC have a father still alive, yet 67% of these men do not live with their child. Twenty-four percent of the OVC have a mother still alive, yet 31% of these women do not live with their child. The most cited reason for this is that the surviving parent must live far away for employment. In regards to the caregivers, there is an even distribution across age ranges and relationship to the child. Finally, 48% reported themselves as a "grandmother" or over the age of 55 years.

Conclusions: To best support children made vulnera-

be the AIDS crisis, data must first be obtained to identify the current profile and needs of these children. Literature concerning OVC in Southern Africa holds that they are living in child-headed or skipped-generation households. The preliminary results of this project show a more complicated family dynamic for a sample of this population. With continued data collection and analysis, results will help guide immediate community action on behalf of the NGO as well as influence future intervention models.

Acknowledgements: Aniset Kamanga, Malaria Institute at Macha, John Spurrer, Macha Mission Hospital, Sten Vermund, Bryan Shepherd and Cathy Jenkins, Vanderbilt University School of Medicine, and Robb Sheneberger, University of Maryland (Baltimore).
The Role of ApoE Polymorphisms in Children with Diarrhea Burdens in Brazil

Olajumoke Fadugba
International Health

Background: Children in poor urban areas of north-east Brazil have among the highest rates of diarrheal illness in the world. It is known that children with repeated diarrheal episodes have significant cognitive impairment and reduced physical fitness. The ApoE4 allele is known to protect cognitive development of these children. ApoE4’s effect on the cardiovascular health of children who suffered severe early childhood diarrhea has not been studied.

Objectives: To determine whether ApoE polymorphisms are a predictor of the physical fitness of children who have experienced high burdens of early childhood diarrhea.

Materials and Methods: The study was conducted in the favela community of Goncalves Dias. The cohort comprised of children with recorded ApoE genotype (three common alleles E2, E3, and E4, determine six genotypes) and recorded number of diarrhea episodes in their first two years of life. Each child underwent the Harvard Step Test (HST), and then heart rate recovery after exercise was monitored. Subjects’ physical activity during a controlled balloon game was also measured using motion detectors. Children’s HST scores and physical activity scores were compared with their ApoE status.

Results: A total of 81 children above age 6 (33 males and 48 females) were studied; there were 9 ApoE2+, 22 ApoE4+, and 45 ApoE3/3 (homozygous) children. The average HST score for ApoE2+ children was 206.87, for ApoE4+ was 188.7, and for ApoE3/3 + was 207.1. Children with ApoE4 genotype have the lowest HST scores.

Conclusion: Children with ApoE4 genotype appear to have lower cardiovascular fitness.

References: Pediatric Research: http://www.pedresearch.org/cgi/content/full/57/2/310

Acknowledgements: Mentors: Sean Moore, MD, and Sten Vermund, MD, PhD, Vanderbilt University School of Medicine, Reinaldo Oria, PhD, and Aldo A.M. Lima, MD, University of Ceara, Brazil, and Richard L. Guerrant, MD, University of Virginia. Co-authors: Ben Kozヤk and Chris Eller. We also thank the health workers and the children who participated in our study.

Risk Factors for Developing Melanoma in the Community of Valencia

Sweeta Ghodasara
International Health

Background: Malignant melanoma is one of few cancers whose rate is still rising throughout the world. While its risk factors have been characterized in numerous studies in fair skin populations, few epidemiological studies have focused on Mediterranean populations, especially Spain, where mortality rate from melanoma remains high.7

Methods and Materials: In this case-control study, we reviewed charts in an electronic melanoma database to identify 290 adult melanoma patients at the Instituto Valenciano de Oncologia who presented with their first melanoma between January 2000 and September 2006. An interviewer conducted a questionnaire to the 290 controls who visited their Centros de Salud (family clinics) between June and July 2006 to evaluate for melanoma. We evaluated phenotypical features, skin type, occupational and educational history, sun exposure history, drinking and smoking habits, number and types of skin lesions, and family and personal histories of cutaneous and other cancers. Spearman’s rho-squared test, chi-squared test and logistic regression were used to statistically analyze the variables.

Results and Conclusions: Univariate and multivariate logistical regression analysis demonstrated increased association of developing melanoma with solar lentigines, chronic sun exposure, personal history of cutaneous skin cancer (basal cell or squamous cell), severe sunburns and multiple melanocytic nevi. Risk also increased with presence of both melanocytic nevi and atypical nevi, with both history of chronic sun exposure and severe sunburns or non-melanoma skin cancer. Data was inconclusive on the effect of smoking and tanning beds on melanoma. No association was seen between hair color, eye color and skin type or between a family history of melanoma and pancreatic cancer.


Obesity in Women of Reproductive Age in a Periurban Area of Lima, Peru

Nina E. Glass
International Health

Background/Problem: Obesity is a growing problem worldwide that is associated with diabetes, cardiovascular disease and other chronic complications. In developing countries like Peru a nutritional transition is occurring in which under-nutrition coexists with obesity. We conducted a study to evaluate the prevalence and potential risk factors for overweight and obesity in women living in a periurban area of Lima, Peru.

Methods and Materials: A cross-sectional house-to-house survey of women aged 20-49 years was conducted in July and August 2006 in Chorrillos, a low to middle income neighborhood in the periurban area of Lima, Peru. Participants reported their perceived weight, food intake and physical activity. Weight and height were measured by anthropometry and the Body Mass Index (BMI=weight in kilograms over height in meters squared) was calculated. Women with recent pregnancy or physical disability were excluded.

Results: Of the 538 women identified in the study area, 56 were ineligible because they had been pregnant in the past 6 months. Completed questionnaires and anthropometric measurements were obtained from 413 of the remaining 482 eligible women (86%). The prevalence of obesity (BMI?30) was 19% and overweight (25?BMI<30) was 36%. The prevalence of obesity increased with age from 6% in women 20-29 to 34% in those 40-49. Neither food intake, physical activity nor accuracy of perceived weight correlated significantly with prevalence of obesity.

Conclusions: This study demonstrates the high prevalence of overweight and obesity in low to middle income women in periurban Lima and raises concerns about future consequences of chronic diseases. A case-control study is planned to more carefully identify risk factors of food intake and physical activity that might provide clues to interventions that could limit this problem. As developing countries begin to face the same challenge of overweight that we see in industrialized nations, we must continue to explore the causes of this newest pandemic, in order to prevent it.

Acknowledgements: Dr. Sten Vermund, Director Vanderbilt Institute for Global Health, Vanderbilt University School of Medicine and Dr. Monica Mispireta and Dr. Claudio Lanata, Instituto de Investigacion Nutricional, Lima, Peru.

The Incidence of Trauma Due to Motor Vehicle Collisions in Ogbomoso, Nigeria

John E. Humphrey
International Health

Background/Problem: Nigeria is the most populous country in Africa with approximately 140 million people. The major mode of transportation between cities is by motor vehicle. Located in southwestern Nigeria, Ogbomoso and environs contain approximately 1 million people. The Baptist Medical Center Ogbomoso (BMCO), is located on a major national highway. Road conditions and high volume traffic lead to many motor vehicle collisions in this area. Motorcycles, providing quick and affordable travel in the city, add to the problem. A large amount of the resulting trauma is seen at BMCO.

Objectives: Discern the impact of motor vehicle collisions (MVCs) on the number of trauma patients seen at BMCO. Describe the contribution of motorcycles to the overall burden of trauma.

Methods and Materials: This study was conducted at BMCO in Nigeria. The patient charts from those involved in MVCs over the past 10 years were obtained from the
Neurological Manifestations of HTLV-1 Infection in Peruvian Children

Emily Kendall
International Health

Background/Problem:
Human T-cell lymphotropic virus type 1 (HTLV-1) is implicated in diseases including infective dermatitis (ID), the most commonly-observed outcome affecting children, and Tropical Spastic Paraparesis (HAM/TSP). The latter affects primarily adults, but several cases of HAM/TSP have been reported in HTLV-1-infected adolescents, particularly those with a history of ID. It is unclear whether neurologically normal-appearing HTLV-1-infected children may also have subclinical abnormalities.

Objectives:
1. To determine if HTLV-1 infection is associated with abnormal neurological or developmental symptoms and exam findings, and to determine if abnormal neurological findings, if present, are associated with a history of ID.

Methods and Materials:
Children ages 3-18 whose HTLV-1-positive were enrolled in a Lima hospital’s ongoing HTLV-I cohort study were included. An initial-at-home survey of children’s medical histories, developmental histories and current neurological symptoms was administered by a blinded investigator, followed by a battery of standardized neuropsychological evaluation. Wilcoxon rank-sum and Pearson chi-square tests were used to test for associations.

Results:
Fifty-four HTLV-1-infected and 40 uninfected children were studied. Infection was associated with lumbar pain, lower extremity weakness, myalgia and myoclonus (p=0.15, 0.08, and 0.06, respectively), and also with clumsiness, Babinski sign and lower extremity hyperreflexia (p=0.02, 0.15, 0.04). Associations with constipation and urinary symptoms were not significant (p=0.90, 0.84), and distributions of developmental milestones did not differ significantly between groups. Among infected children, history of infective dermatitis was loosely associated with abnormal lower extremity pyramidal signs (p=0.14), urinary symptoms (p=0.32), and constipation (p=0.67).

Conclusions:
HTLV-1-infected children require close follow-up for relatively frequent, abnormal neurological findings.

References:
A Retrospective Study of Trauma for a Ten Year Period at a Nigerian Hospital

Michael K. Fasten
International Health

Background/Problem: Trauma has been an increasing problem worldwide, especially in Nigeria and other developing countries. In these developing countries, research goals have been directed towards infectious diseases leaving a gap in trauma research. This study hopes to bring some light to the impact and the types of injuries caused from trauma by investigating patients seen at the Baptist Medical Center, Ogbomoso (BMCO), Nigeria, a tertiary care hospital located on a major highway. Using the research at one hospital will hopefully provide an example of the prevalence of trauma for the larger community.

Objective: To assess the types of injuries caused by trauma and treated at BMCO.

Methods and Materials: All trauma cases of all ages from BMCO over a 10-year period from January/February (dry season) 2006 to July/August (rainy season) 1996 to January/February (dry season) 2006 were recorded using a Microsoft Excel spreadsheet. The investigators read through the trauma patients’ charts and extracted the following data: age, sex, rainy/dry season, year of trauma, presenting diagnosis, type of trauma, and cause of trauma.

Results: A total of 980 separate entries were recorded for the 10 year period with 720 being inpatient and 260 being out-patient. The average percentage of trauma inpatients from all inpatients was 5.4%. For all outpatients, the average number of trauma outpatients was 0.20%. The main cause of trauma was motor vehicle collisions (83%). The main types of trauma were fractures (40%) and lacerations (33%). Of the total cases, 8.2% were reported as deaths.

Conclusions: The majority of trauma cases were motor vehicle collisions with the main type of injury being fractures. The percentage of inpatient trauma cases and reported deaths were lower than expected.

Acknowledgements: To my co-investigators: Mr. Humphrey at Vanderbilt University Medical Center and Dr. John Tarpley, Mrs. Margaret Tarpley and Dr. Peter Wright, Vanderbilt University Medical Center, Mr. Iyere, Dr. Adeleke and Mr. Oladunjoye, Baptist Medical Center, Ogbomoso, Nigeria.

A Comparison of Neonatal Transport Systems

Jill Wilmoth
International Health

Background/Problem: Vanderbilt Children’s Hospital (VCH) has spent over 30 years developing a neonatal transport system which has successfully opened communication between regional and outlying hospitals, resulting in decreased neonatal morbidity and mortality and promotion of early and frequent consultation. This system will serve as a model for comparison and improvement of the neonatal transport system at Hospital Nacional de Niños (HNN) in Costa Rica. As a product of this study, recommendations will be made for the neonatal transport system in Costa Rica.

Objectives: To compare the neonatal transportation systems at VCH and HNN and to implement improvements in Costa Rica.

Methods and Materials: The year 2005 was selected for comparison. At HNN, 573 patients were transported from outlying hospitals and 122 patient charts were reviewed. The variables reviewed were divided into four categories. Variables in the first category included demographic characteristics, the second represented stabilization measures performed before admission to HNN, the third was based on clinical and laboratory assessment performed upon admission to HNN, and the fourth included transport-related mortality and morbidity and final disposition.

Results: There was a significant amount of very low birth weight (18%) and very premature infants (26%) transported to HNN. A majority of patients were transported due to respiratory insufficiency (67.5%) and sepsis (26.8%). Compared to Vanderbilt, a high percentage of patients at HNN had hyperthermia (21%), were coded during transport (39%), and died (13.8%) during their first hospitalization.

Conclusions: These results suggest that further stabilizing measures are needed prior to and during transport in order to prevent these complications. Further statistical analyses are being performed to describe additional features of the neonatal transport system in Costa Rica and, based on the full analysis, recommendations will be formulated which will serve as a basis for improvement of the neonatal transport in Costa Rica.

Acknowledgements: Mentor: Dr. Mario Rojas MD, MPH, Vanderbilt Children’s Hospital; mentor in Costa Rica: Dr. Carlos Castro Herrera, Chief of Neonatology, Hospital Nacional de Niños

HIV and Syphilis Testing Among Adolescents and Youth in Port-Au-Prince, Haiti

John Wood
International Health

Background: More than 50% of the new 4.9 million HIV infections in 2005 worldwide occurred in adolescents (12-17 years old) and youth (18-25 years old) with nearly three quarters of these infections in Sub Sahara Africa and the Caribbean occurring in young women. The both of these locations, young women experience a higher rate of infection not only due to biological differences, but also more significantly, due to gender inequality. Young women are coerced to have sex with older men both by the threat of violence and the increasingly described phenomenon of transactional sex for food, clothing and shelter. One recent study performed on Haiti’s Central Plateau reported that 68% of women 30 years old or younger had experienced forced sex during their lifetime, while another stated that over 12% of males aged 15-19 who had been sexually active in the 12 months preceding the survey reported having had sex with a commercial sex worker. HIV/AIDS accounted for more deaths among 10-19 year olds than any other single cause in Haiti in 1999, and although more recent data suggests that while overall HIV prevalence is declining, this vulnerable population may not be experiencing the same decline in disease as the overall Haitian population. Current studies have indicated that the decline in HIV/AIDS is largely due to mortality and blood screening and may be largely restricted to urban areas. Furthermore, HIV-infected adolescents and youth on ART have poor adherence and high rates of virologic failure with drug-resistant virus and are at risk for disease progression and death. They engage in unprotected sex and remain at risk for HIV-1 transmission to their infants and sexual partners.

Objectives: We describe 30,446 youth and adolescents who presented for voluntary counseling and testing (VCT) for HIV and syphilis (RPR) at GHESKIO clinic in Port Au Prince, Haiti between 2001 and 2005. Trends were evaluated for testing across time, age, sex, and pregnancy status.

Methods and Materials: We are using questionnaire data and HIV/RPR test results that are collected in VCT services at GHESKIO. The study is a cross-sectional survey of persons ages 12-25 years presenting for counseling and testing. However, attempts to use change over time in testing from 2001 to 2005 were used to make longitudinal approximations.

Results: While overall recruitment significantly increased across all groups during the testing period, it was most profound in female youth without an associated significant increase in number of positive HIV tests. Therefore, the overall
prevalence in the test group declined. Furthermore, this decline is more dramatic for the GHESKIO sample group than in national surveys leading us to hypothesize that either recruitment bias or mandatory testing of pregnant women was responsible for the rapidly decreasing incidence in the test population. It should be noted, however, that HIV incidence was 6.8-7.2% higher in the test population that in national estimates for all years. Further analysis revealed that non-pregnant women were the primary source of negative tests and the most significant reason for declining HIV rates in the test population. Also, HIV prevalence was similar and relatively stable among both male (6.58%) and female (6.67%) adolescents, but as age increased beyond 17 years, female prevalence increased much more rapidly than in males. RPR rates behaved similarly and have been well documented elsewhere as significant cofactors in the HIV epidemic. Additionally, syphilis is a significant source of morbidity and mortality regardless of HIV status.

Conclusions:

The data suggest that while recruitment at GHESKIO is excellent and far more efficient than the national testing, its decreasing efficiency is most likely as a result of recruitment bias. While HIV and RPR prevalence are similar among adolescent males and females, the rapid increase in female youth indicates that during the adolescent years, females are being infected much more rapidly than males. RPR rates behaved similarly and have been well documented elsewhere as significant cofactors in the HIV epidemic. Additionally, syphilis is a significant source of morbidity and mortality regardless of HIV status.

Evaluating Routine Antenatal Care at Korle Bu Teaching Hospital, Ghana

Shormeh Yehoah

International Health

Background/Problem:
The high perinatal mortality rate has been a major concern in Ghana. Studies show that a large proportion of mortality is preventable, and is attributable to errors by health-care workers and departures from accepted standards of care. The evaluation of healthcare practices could target interventions aimed at improving standards of care and reducing high rates of mortality.

Objectives:
To assess the current antenatal care practices at the Korle Bu Teaching Hospital (KBTH), Accra, Ghana, and to determine women’s perceptions of the care provided.

Methods and Materials:
This study was conducted over a six week period at a teaching hospital in Accra, Ghana. A systematic sample was chosen from current patents in the maternity unit and their charts reviewed for evidence of specific indicators of standard care received during three antenatal visits. In addition, a descriptive survey was administered to a random sample of patients to determine their level of satisfaction with the care provided.

Results:
One hundred thirty-one patient charts were reviewed. Blood pressure, maternal weight, gestational age and urinalysis tests were the top four indicators most consistently recorded at each of three visits reviewed per patient. Hemoglobin, iron supplementation and ultrasounds were the least consistently recorded. Ninety-five women were surveyed. Ninety-two percent indicated satisfaction with the services they received; however, 50% of these also expressed some dissatisfaction, mainly with treatment by the nurses, and the amount of time spent at each visit.

Conclusions:
A thorough evaluation of specific practices in the delivery of antenatal care is needed to identify weaknesses and determine ways to better serve the patient population in this setting.

Acknowledgements:
Dr. Sten Vermund, Vanderbilt University School of Medicine and Dr. K. Nyekyera, Korle-Bu Teaching Hospital, University of Ghana Medical School.

Laboratory-Based Biomedical Research

Experiences in the area of Laboratory-Based Biomedical Research are focused on hypothesis-driven investigation in a basic 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.

Lillian Namney, 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 hyperproliferative 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. Namney’s contributions extend to the national level where she recently served as the national president of the Wound Healing Society.

“Directing the lab-based Emphasis area was quite an adventure for me and the 21 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 an 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 richer appreciation for the behind-the-scenes efforts and serendipity that goes into the discovery process that shapes the future of medicine.”
Investigation of Protein Expression Patterns in a Rodent Model of Manganese Neurotoxicity

Douglas Anderson
Laboratory-Based Research

Background/Problem: Manganese is an essential trace element, however, in excess it causes a Parkinson-like disorder characterized by movement difficulties and psychiatric symptoms. The toxic effects of manganese are predominantly seen in miners and welders; however, its use as a gasoline additive and parental nutrition fluids may cause other exposures. The mechanism of manganese toxicity is not well understood.

Objectives: To investigate markers of cell stress and function to discover candidate pathways for manganese toxicity.

Methods and Materials: Cell lysates from the brain stem, cortex, cerebellum, hippocampus, mid-brain, olfactory bulb and striatum of rats treated with either manganese chloride (5 mg/kg IV daily) or a saline control were used for western blots using antibodies for HSP70, parkin, cleaved caspase 3, tyrosine hydroxylase (TH), HSC70, and α-tubulin. Sections including the substantia nigra were stained for TH to investigate dopamine synthesis in the substantia nigra.

Defects in Islet Vascularization in Animal Model of Type II Diabetes

Brigham An Lab, Laboratory-Based Research

Background: Pancreatic islets receive 5-10 times more blood flow than surrounding pancreatic acinar tissue, suggesting that blood flow to the islet is essential to proper islet function. Islets also have capillaries that are fenestrated, allowing easier passage of the molecules that help to regulate the release of hormones like insulin and glucagon. The partial pressure of oxygen is higher in islets than in exocrine pancreas. These distinctive features of the vasculature of a healthy pancreas prompted the investigation of vascular parameters in a type 2 diabetes model.

Conclusions: The western blot revealed only one significant change in protein expression. The immunohistochemistry seems to indicate a significant effect on dopamine synthesis in the substantia nigra.

Acknowledgments: I would like to thank my mentor Dr. Michael Aschner. I also appreciate the help from Dr. Vanessa Finsanakis, Dr. Gregg Stanwood, George Jiang and the entire Aschner lab.

Hypothesis: Defects in islet vascularization contribute to the islet dysfunction seen in type 2 diabetes. The hypothesis was tested by comparing the pancreatic vasculature in type 2 diabetic mice against the control.

Methods and Materials: Db/db (n=7) and heterozygote (n=4) mice at 2 months of age were injected with tomato seed lectin 5 minutes prior to pancreas removal and fixation with 4% paraformaldehyde. Ten µm sections were collected from three different depths of the tissue block spaced by 200 µm. Sections were then mounted with DAPI mounting medium and examined using an Olympus BX41 camera and Metamorph software.

Results: Islets in db/db mice were significantly larger than those in heterozygote mice (26180 ± 16290 vs. 16290 ± 1277, p = .0005). However, islets from db/db had reduced islet vessel density (#vessels/mM², 1000 ± 17.4 vs. 1513 ± 51.78, p = .0001) and decreased vessel area (vessel area/mM², 75.90 ± 2.487 vs. 109.7 ± 7.301, p = .001) when compared to the heterozygote group.

Acknowledgements: I would like to thank the entire Aschner lab.
Background: In modern radiotherapy, structures are delineated on a CT or MR scan in order to avoid damage to sensitive areas. Currently, organ borders are manually drawn by experts using a computer, which is time-consuming. In previous work, brain structures were delineated on a CT or MR scan in order to avoid damaging the patient’s head with the head rest during scanning. The patient’s head is then positioned supine or prone and the patient is moved on the bed to the desired location. The patient’s head is then maintained in a fixed position relative to the head rest during the procedure. It is possible to accurately delineate large structures such as the cerebellum, but delineation of smaller structures such as the optic nerves and chiasm was less successful.

Methods: Points on the border of the nerves and chiasm were marked on several “atlas” images and then projected onto the patient’s image using an elastic “atlas” images and then projected onto the patient’s image using an elastic deformation algorithm. Corresponding points’ locations were averaged and a smooth border was generated from the patient’s image using an elastic deformation algorithm. In resecting a neurosurgical brain tumor, the surgeon is faced with the difficulty of orienting the patient’s head to maximize the success of removing the pathology. Currently, these decisions are based on the experience of the surgeon.

Objective: To develop fully automatic computer software which accurately delineates the optic nerves and chiasm on CT images alone.

Conclusions: Accurate automatic delineation of small, low-contrast structures is achievable using CT images alone.

References:
D’Haeze PF, et al. Atlas-based segmentation of the brain for 3-dimen-

Acknowledgements:
My mentor for this work was Benoit Dauwant in the Department of Electrical Engineering and Computer Science. Anthony Cmelak and Kenneth Niermann, in the Department of Radiation Oncology, contributed organ contours and provided evaluation of our method’s results.

Results: Positioning the patient supine results in the least amount of intra-operative deformation. For tumors in close proximity of the falk cerebi, rotating the patient’s head with the head rest
ing on the side results in a greater amount of deformation, but it also results in better tumor exposure and greater tensile stress at the tumor-brain interface, facilitating surgical resection.

Fig. 1: Representative results. Anterior view. Superior part of the skull has been cut away for sake of visualization.

Modeling Surgical Procedures to Assist in Understanding Surgical Approach

Kevin Hl Laboratoy Based Research

Background/Problem:
In resecting a neurosurgical brain tumor, the surgeon is faced with the difficulty of orienting the patient’s head to maximize the success of removing the pathology. Currently, these decisions are based on the experience of the surgeon.

Objective: The objective is to demonstrate the clinical potentials of computer simulation for assisting surgeons determine the optimal surgical approaches by providing them with an understanding of the biomechanics of brain deformation.

Methods and Materials: Computer simulation is used to quantitatively assess the advantages and disadvantages of a series of surgical approaches with various head orientations. Each approach is evaluated for the extent of tumor exposure and the level of stress at the brain-tumor interface, both of which are reliable indicators of the ease of resection.

Results: The –actinin-1 knockdown cell line was infected with RSV, a 70,000-fold reduction in free virus was observed. There was only a four-fold reduction in cell-associated virus. We observed an apparent elongation of viral inclusions on infected cells in images acquired by confocal microscopy.

Conclusions: Our model can help surgeons determine the optimal surgical approach that uses naturally-occurring forces to facilitate tumor exposure and resection.

References:

Acknowledgements: Mentor: Michael Miga, Department of Biomedical Engineering. Prashanth Dumpari, Department of Neurosurgery, and Reid Thompson, all Vanderbilt University Medical Center.

Host Determinants of Assembly and Budding of Respiratory Syncytial Virus

Josh M. Heck Laboratory-Based Research

Background: Human Respiratory Syncytial Virus (RSV) is recognized as the most important viral cause of serious pediatric respiratory tract infection worldwide. While it has been observed that RSV preferentially buds from the apical surface of infected polarized epithelial cells, little is known about the mechanism. Previously our laboratory has shown that proper function of the apical recycling endosome (ARE) is required for completion of the RSV life cycle. Further work demonstrated that two proteins required for proper function of the ARE, myosin Vb and Rab11-FIP2, are required for assembly and budding respectively, but no direct interaction with viral proteins has been detected. Our recent proteomic analysis of the ARE yielded a list of possible interacting proteins, which may act on the late steps of the RSV life cycle.

Objectives: To determine which apical recycling endosome (ARE) associated proteins play a role in RSV assembly and budding.

Methods and Materials: It was determined that one ARE associated protein, –actinin-1, localized in two viral structures, cytoplasmic inclusion bodies and cell-surface filaments. We stably transfected human bronchial epithelial (HBE) cells with a plasmid encoding an shRNA directed against –actinin-1. We studied the effect that these knockdowns had on the viral life cycle using cell culture and viral infections, laser scanning confocal microscopy and scanning electron microscopy.

Results: When the –actinin-1 knockdown cell line was infected with RSV, a 70,000-fold reduction in free virus was observed. There was only a four-fold reduction in cell-associated virus. We observed an apparent elongation of viral inclusions on infected cells in images acquired by confocal microscopy.

Conclusions: These data suggest that –actinin-1 localizes to viral inclusions and filaments and is required to facilitate a late step in RSV filamento budding from the apical plasma membrane.

Acknowledgements: Thomas J. Usery and James E. Crowe, Jr., Departments of Pediatrics and Microbiology and Immunology, Vanderbilt University School of Medicine.
allosteric potentiator analogs of Type III metabotropic glutamate receptors. Methods and Materials: Cells were co-transfected with the specific receptor and expression vectors for the transducer subunits in transient transfection assays. The transduction signal was measured using Fura-2/AM imaging.

Results: Several analogs of MPEE (a known allosteric potentiator of mGlur4) were identified as novel potentiators or antagonists of mGlur4 including YP270, YP270, and YP318. Several analogs of PHEC (another known allosteric potentiator) were also found to have novel potentiating or antagonistic effects.

Conclusions: The GIRK assay is a sensitive, specific, and cost-effective method to study mGluR4 and mGluR8. The compound activity and potentiator (or antagonist) were identified in the basal ganglia motor circuit.

Acknowledgments: Co-authors: David J. Calkins, PhD and Rebecca M. Sappington, PhD, Vanderbilt Eye Institute.

Acknowledgements: Co-authors: David J. Calkins, PhD and Rebecca M. Sappington, PhD, Vanderbilt Eye Institute.

Introduction: The purpose of this study was to determine the effects of surface roughness and hardness on tissue response, as measured by contact angle, of retrieved cobalt-chromium alloy (CoCr), yttria-stabilized zirconia (Y-TZP), and magnesium-stabilized zirconia (Mg-PSZ) femoral heads. Lower contact angles generally mean higher wettability and enhanced lubrication, which should lead to decreased wear in vivo. In an inverse relationship was hypothesized between contact angle and root-mean-square (RMS) roughness (Sq), which tends to be more sensitive to scratches that could help flatten a water droplet. Because metals like CoCr have a lower hardness than ceramics used as bearing surfaces, CoCr heads were expected to scratch more easily and roughen with age, thus exhibiting a higher contact angle. The roughening of Y-TZP with age in vivo is well-documented, while Mg-PSZ does not roughen with age, so contact angle was expected to increase with age in vivo for only Y-TZP zirconia heads.

Methods and Materials: CoCr (n = 16), Y-TZP (n = 18), and Mg-PSZ (n = 17) femoral heads were retrieved from total hip arthroplasty revision surgeries, and non-implanted control specimens (n = 4-5 each) were donated by Whiteside Biomechanics, Inc. Retrievals were cleaned with a bleach solution and thoroughly rinsed with water and ethanol. Average (Sa) and RMS (Sq) roughness were measured by optical profilometry at magnifications of 32x and 10x at three locations per specimen. Relative wettability was measured by the sessile drop method; the average contact angle, as measured by the sessile drop method, was less than 0.25 µL of distilled water after a methanol-aceton alcohol wash. Retrievals were then washed in an enzymatic detergent, rinsed in distilled water and re-measured. Only the final 10 of 20 droplets per specimen were analyzed to minimize the influence of residual organic material. Roughness and contact angle data were correlated to age in vivo and each other, and contact angle data were compared using paired t-tests (p < 0.05).

Results and Discussion: The contact angle of the retrieved femoral heads increased exponentially with age in vivo (p < 0.001 at 32x and 10x), while Mg-PSZ did not roughen with age. For all three material types, contact angle (both wash methods) was not significantly correlated to age in vivo or to surface roughness, even using the most conservative measure of roughness (Sq at 10x, representing an area of 633 µm x 476 µm, only slightly smaller than a droplet’s footprint). For hydrophilic surfaces, contact angle is inversely proportional to surface roughness via Young’s equation, but the range of roughness measurements was probably too small to produce significant differences.

After averaging all contact angle data by material type (Table 1), the contact angle of retrievals (post-alcohol wash) was significantly lower than corresponding never-implanted controls (unpaired t-test), but contact angle significantly increased after enzymatic washing (paired t-test). After the enzymatic wash, only the CoCr retrievals still had a contact angle significantly lower than controls, suggesting that the wash removed a residual film left-over from joint fluid in vivo. Because contact angle was not correlated to age in vivo, the data imply that this film was created within weeks of implantation, with material surface chemistry only affecting how fast or perhaps how strongly the film is formed. The CoCr contact angle data suggest that the enzymatic wash incompletely removed any leftover residual film, but differences may have also been due to various ASTM standards for CoCr alloy among the eight different manufacturers represented.

Conclusions: To the best of the authors’ knowledge, this is the first study to measure the contact angle of retrieved femoral heads. The apparent residual film removed by enzymatic washing implies that joint fluid (or film), which increases the wettability of the bearing surface regardless of substrate material used. Future studies will attempt to recreate this residual film on never-implanted specimens.
Analysis of MCCC1 and MCCC2 Genes of Infants Whose Screening Results are Suggestive of 3MCCD

Phillip B. McWhorter  Laboratory-Based Research

Introduction:
MS/MS newborn screening (NBS) detects elevated 3-hydroxyisovaleryl carnitine (3C10H) which is associated with 3-Methylcrotonyl CoA Carboxylase Deficiency (3MCCD). While often asymptomatic, some infants with 3MCCD present with hypotonia or a Reye-like illness. Reported incidence is about 1:50,000 with no known high risk populations.

Hypothesis:
Variations in MCCC1 and 2 genes are associated with elevated 3C10H on NBS in middle Tennessee, especially among Hispanic and Kurdish populations.

Methods and Materials:
MCCC1 and 2 transcripts were sequenced for those with repeated 3C10H elevations on NBS and frequencies of variations were determined in controls.

Results:
From July 2004 to February 2007, 107 neonates had 3C10H elevations on their NBS. Of these 107% were evaluated because they also had 3-OH-isovaleric acid (3OHIA) elevations suggestive of 3MCCD. Ethnicity was 53% American, 18% Hispanic, 18% African American, and 12% Kurdish (all consanguineous). Sequencing MCCC1 and 2 RT-PCR products from lymphoblastoid treated with puromycin to prevent NMD identified novel mutations in each. Case 1 was heterozygous for a single G deletion (I073delG) that is predicted to cause a frameshift starting with codon 358 of MCCC1. Case 2 was heterozygous for a 2bp deletion (640-641delGG) that also causes a frameshift and results in NMD of MCCC1 transcript. Case 3 was homozygous for a G to A transition (G1015A) encoding a Val339Met substitution in the MCCC2 gene. No MCCC1 I073delG or MCCC2 Met339 alleles were detected in 200 control alleles.

Conclusions:
1. Elevated 3C10H and 3OHIA were seen in ~13800 births. 2. Hispanics and Kurds comprise 30% of our cases but less than 1.3% of our population. 3. All of our first three samples analyzed showed rare allelic variants in MCCC1 or 2 that are plausible causes of perturbed 3MCC function. 4. Determining the mechanisms by which these variations perturb 3MCC expression or function will require further studies.

Acknowledgements:

Pretreatment with cyclophosphamide decreased the effect of postnatal saporin, a ribosome-inactivating protein, which plays a major role in the regulation of an apoptotic response to cell damage. BID is also thought to play an intermediate role between FAS receptor signaling and mitochondrial BAX and BAK. Additionally, BID has been shown to have an ATM-mediated role in the intra-S phase checkpoint.

Objectives:
To assess what determines BID’s localization within the cell and what impact localization has on cell survival.

Methods and Materials:
Fluorescent microscopy was used with mouse embryonic fibroblasts (MEFs) to determine localization in response to etoposide, hydroxyurea or no treatment. Wild type cells (C9), BH3 mutants deficient in the apoptotic domain (3478), and mutants deficient in the cell cycle checkpoint (578A), were exposed to each treatment and BID localization was evaluated.

Results:
We found that wild-type (C9) BID localizes to the nucleus in response to treatment with DNA damage agents. In addition, the 578A mutants showed increased mitochondrial localization though nuclear localization was not prohibited. Finally, the BH-3 mutation does not prohibit BID localization to the mitochondria, though more nuclear localization is seen as hypothesized.

Conclusions:
Wild-type and 3478 mutants exhibited a propensity towards cell cycle repair pathway localization to the nucleus. Despite this, experiments with BH-3 mutants showed that BAX and BAK do not appear to be essential for BID localization to the mitochondria. Finally, more BID is present in the apoptotic pathway with the 578A mutant BID, though some nuclear localization indicates that cell-cycle repair checkpoint activity may also be present.

Assessment for T-Regulatory T-Cell Expression in Sarcoidosis Patients Induced by M. Tuberculosis Ag85A
Shaneel M. Miller  Laboratory-Based Research

Background:
Sarcoidosis is an immune system disorder characterized by non-caseating, non-necrotizing granulomas. Patients with active disease exhibit energy to many common pathogens (Candida, Tetanus, etc.). A prior report shows sarcoid patients from France have increased expression of CD4+ CD25+ T cells compared to controls (Miya et al. JEM 2006).

Objectives:
To investigate for the presence of increased T regulatory expression in Sarcois sarcoid patients in response to M. tuberculosis Ag85 in all these groups causes no significant change in T reg expression within each group but did result in more similar T reg expression between the groups.

References:

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Descending Serotonergic Modulation of Nociception
Samuel Arthur Moore  Laboratory-Based Research

Background:
The transmission of nociceptive signals from the spinal cord to cortex has long been known to be influenced by descending serotonergic projections originating from the hindbrain raphe system. However, most of the evidence regarding this system has been based on postynaptic receptor agonist/antagonist studies and, at times, has been contradictory. No group has sought to selectively destroy the descending serotonergic raphe neurons to observe the effects of such an input loss.

Objectives:
To selectively ablate serotonergic neurons projecting to the lumbar enlargement dorsal horn using an intrathecal injection of a selective neurotoxin, SERT-Sap and to observe the behavioral consequences and anatomical correlate of such a lesion.

Methods and Materials:
SERT-Sap, a neurotoxin consisting of a serotonin transporter antibody conjugated to saporin, a ribosome-inactivating peptide, was injected into the lumbar cistern of Sprague-Dawley rats. Two weeks post-operation, the animals were investigated for changes in nociceptive behavior using a formalin test. Immediately following formalin testing, the rats were sacrificed. Their lumbar enlargements and hindbrains were removed for cytochemical staining.

Results:
Although behavioral data suggest a difference between SERT-Sap treated and control rats, with SERT-Sap leading to a marked reduction in nociceptive behavior, no statistical significance has as of yet been found. Recently, the SERT-Sap dose has been raised to its maximal level in hopes of eliciting a significant behavioral result. No cytochemical data on the anatomical effects of SERT-Sap administration are currently available.
To identify the specific amino acid mediated APOBEC3G degradation protein interactions that govern Vif-targeting it for proteasomal degradation. While it is known that Vif is targeting it for proteasomal degradation, the role of histone deacetylase (HDAC) in this process is less well understood. In this study, we sought to investigate the role of HDACs in Vif-mediated degradation of APOBEC3G.

Methods and Materials: Mutations were introduced into the entire sequence of the HIV-1 Vif gene using a PCR-based random mutagenesis procedure. Mutated Vif sequences were ligated into the eukaryotic expression vector pcDNA3.1 (+) and transformation of E. coli was used to generate 204 mutant Vif clones with a mutation frequency of 1.07 nucleotides per clone as determined by DNA sequence analysis. Mutant clones with mutations occurring within three regions of Vif (amino acid residues 3–31, 100–115, and 145–160) previously identified as potential mediators of the Vif-APOBEC3G interaction were screened for impairment of Vif-induced APOBEC3G degradation by Western blot analyses.

Results: Western blot analyses identified six mutant clones with impaired ability to induce APOBEC3G degradation. Mutations were detected within all three regions of Vif described above.

Conclusions: Preliminary data generated using this functional screening assay suggests that multiple sites on Vif may mediate its interaction with APOBEC3G.

Acknowledgments: This work was supported by National Institutes of Health Grants AI101820 and AI87833 to J. Tollefson. A. A. F. is supported by a NARSAD Young Investigator Award. J. T. is supported by a Howard Hughes Medical Institute Predoctoral Fellowship and the P30 AI51345 training grant.

Identification the HIV-1 VIF Binding Site for APOBEC3G

Nizar A. Mukhtar
Laboratory-Based Research

Background: The HIV-1 viral infectivity factor (Vif) has been shown to counteract the actions of the cytidine deaminase APOBEC3G, an endogenous inhibitor of retroviral replication. Functioning as a substrate receptor, HIV-1 Vif recruits an E3 ubiquitin ligase complex to polyubiquitinate APOBEC3G, thereby targeting it for proteasomal degradation. While it is known that Vif is required by HIV for the productive infection of its primary target cells, current understanding of the host-virus protein interactions that govern Vif-mediated APOBEC3G degradation remains limited.

Objectives: To identify the specific amino acid residues in HIV-1 Vif that are involved in binding APOBEC3G.

Methods and Materials: Mutations were introduced into the entire sequence of the HIV-1 Vif gene using a PCR-based random mutagenesis procedure. Mutated Vif sequences were ligated into the eukaryotic expression vector pcDNA3.1 (+), and transformation of E. coli was used to generate 204 mutant Vif clones with a mutation frequency of 1.07 nucleotides per clone as determined by DNA sequence analysis. Mutant clones with mutations occurring within three regions of Vif (amino acid residues 3–31, 100–115, and 145–160) previously identified as potential mediators of the Vif-APOBEC3G interaction were screened for impairment of Vif-induced APOBEC3G degradation by Western blot analyses.

Results: Western blot analyses identified six mutant clones with impaired ability to induce APOBEC3G degradation. Mutations were detected within all three regions of Vif described above.

Conclusions: Preliminary data generated using this functional screening assay suggests that multiple sites on Vif may mediate its interaction with APOBEC3G.

Acknowledgments: Richard T. D’Aquila, MD, and John P. Donahue, PhD. Department of Medicine, Vanderbilt University Medical Center.

VTFB1 Polymorphisms Modulate Familial Pulmonary Arterial Hypertension in BMPR2 Mutation Heterozygotes

Justin Poling
Laboratory-Based Research

Background: FPAH is a progressive disease with occlusion of the smallest pulmonary arteries, right heart failure and early death. Heterogeneous BMPR2 mutations cause FPAH. BMPR2 encodes a cellular receptor in the TGF Superfamily. The BMP and TGF pathways act through different downstream SMAD pathways. Two TGFβ1 SNPs (–509 C to T and codon 10 T to C) both increase expression and circulating levels of TGFβ1.

Methods and Materials: Determine if these TGFβ1 SNPs modulate the penetrance and/or age of onset of FPAH.

Objective: Determine if these TGFβ1 SNPs modulate the penetrance and/or age of onset of FPAH.

Methods and Materials: We sequenced genomic DNAs from 107 individuals with BMPR2 mutations and determined the relationship between the TGFβ1 haplotypes and FPAH penetrance.

Results: Individuals heterozygous for a BMPR2 mutation and CC, CT or TT -509 TGFβ1 SNP genotypes had 61, 79 and 100% penetrance, respectively. Those with TT, CT or CC TGFβ1 codon 10 SNP genotypes had 52, 78 and 89% penetrance, respectively. Those with 4 or 3, 2, 1 or 0 wild type -509 and codon 10 SNP alleles had 50, 60, 72 and 100% penetrance of FPAH, respectively.

Conclusions: The TGFβ1 SNP genotypes are associated with the penetrance and age of onset of FPAH in BMPR2 mutation positive individuals. This result may be due to exacerbating the imbalance between the TGF and BMP pathways.

Acknowledgements: John A. Phillips III, Division of Medical Genetics, Vanderbilt University School of Medicine.

Structural Characterization and Immunogenicity of the hMPV G Protein

Alex Ryder
Laboratory-Based Research

Background: Neutralizing epitopes of the hMPV G protein are critical targets for vaccine design. Over the past few decades of effort, no successful vaccine has been developed, and no rapid diagnostic test is available to facilitate prompt administration of proper treatment exists. The use of peptide-nanocluster conjugates to structurally mimic a known neutralizing epitope of the virus represents a novel approach to detector and vaccine design.

Objectives: To synthesize peptide-nanocluster conjugates such that the peptide adopts a confirmation immunologically indistinguishable from that of the epitope in the native protein, and to analyze the effect of nanocluster diameter on achieving this goal.

Methods and Materials: The hMPV G protein ectodomain coding sequence was restricted cloned into a mammalian expression plasmid vector containing a cleavable IgG leader sequence and an affinity purification tag. This construct was transiently transfected into 293-F cells and secreted G protein was purified by affinity chromatography. Immunization studies were performed using a well-characterized cotton rat model of hMPV disease and immunity. Groups of animals were immunized twice with either PBS, purified G protein alone, or G protein adjuvanted with TiterMax gold, or were infected once with hMPV. Animals were challenged with live hMPV at 28 days and tissue virus titers will be determined on day 32. Cytokine responses will be determined by ELISA and real-time RT-PCR, and histological analysis will be performed on lung tissues.

Results: The cloning and expression strategy resulted in the successful production of soluble G protein of the correct predict molecular weight. The recombinant G was >95% pure, glycosylated and the typical yield was ~150 µg/60 ml culture. Ongoing experiments will elucidate the degree to which O- and N-linked glycosylation contributes to the molecular weight, oligomerization and immune recognition of G protein. Immunization studies will determine the effect of vaccinating animals with different formulations of G protein on upper and lower respiratory tract pathogenesis and viral loads subsequent to hMPV challenge, thus establishing the ability of G to elicit neutralizing and protective antibody responses.

Conclusions: We developed a novel method for the successful expression of highly pure G glycoprotein. The findings of this work will determine the protective efficacy of hMPV attachment G protein as an hMPV vaccine. These results will provide reagents and a foundation for further studies of G structure and the role of G in pathogenesis and immunity.

Acknowledgments: Mentor: John V. Williams, MD, Division of Pediatric Infectious Diseases, Vanderbilt University School of Medicine. Co-authors: Sharon Tolleson, Amy Herrigars, Gabriella Cseke, PhD, MS and John V. Williams, MD. Support provided by Vanderbilt University School of Medicine and Infectious Diseases Society of America.

Neutralizing Epitope of Respiratory Syncytial Virus

Lauren A. Weigand
Laboratory-Based Research

Background: Respiratory syncytial virus (RSV) is a significant cause of morbidity and mortality in neonates. Despite decades of effort, no successful vaccine has been developed, and no rapid diagnostic tool to facilitate prompt administration of proper treatment exists. The use of peptide-nanocluster conjugates to structurally mimic a known neutralizing epitope of the virus represents a novel approach to detector and vaccine design.

Objectives: To synthesize peptide-nanocluster conjugates such that the peptide adopts a confirmation immunologically indistinguishable from that of the epitope in the native protein, and to analyze the effect of nanocluster diameter on achieving this goal.

Methods and Materials: The hMPV G protein ectodomain coding sequence was restricted cloned into a mammalian expression plasmid vector containing a cleavable IgG leader sequence and an affinity purification tag. This construct was transiently transfected into 293-F cells and secreted G protein was purified by affinity chromatography. Immunization studies were performed using a well-characterized cotton rat model of hMPV disease and immunity. Groups of animals were immunized twice with either PBS, purified G protein alone, or G protein adjuvanted with TiterMax gold, or were infected once with hMPV. Animals were challenged with live hMPV at 28 days and tissue virus titers will be determined on day 32. Cytokine responses will be determined by ELISA and real-time RT-PCR, and histological analysis will be performed on lung tissues.

Results: The cloning and expression strategy resulted in the successful production of soluble G protein of the correct predict molecular weight. The recombinant G was >95% pure, glycosylated and the typical yield was ~150 µg/60 ml culture. Ongoing experiments will elucidate the degree to which O- and N-linked glycosylation contributes to the molecular weight, oligomerization and immune recognition of G protein. Immunization studies will determine the effect of vaccinating animals with different formulations of G protein on upper and lower respiratory tract pathogenesis and viral loads subsequent to hMPV challenge, thus establishing the ability of G to elicit neutralizing and protective antibody responses.

Conclusions: We developed a novel method for the successful expression of highly pure G glycoprotein. The findings of this work will determine the protective efficacy of hMPV attachment G protein as an hMPV vaccine. These results will provide reagents and a foundation for further studies of G structure and the role of G in pathogenesis and immunity.

Acknowledgments: Mentor: John V. Williams, MD, Division of Pediatric Infectious Diseases, Vanderbilt University School of Medicine. Co-authors: Sharon Tolleson, Amy Herrigars, Gabriella Cseke, PhD, MS and John V. Williams, MD. Support provided by Vanderbilt University School of Medicine and Infectious Diseases Society of America.
Comparing the Effects of Etoposide and its Derivatives on Topoisomerase IIα and Topoisomerase IIβ

William Yi
Laboratory-Based Research

Background/Problem: Etoposide, an important anticancer agent, is front-line therapy for a variety of human malignancies. The drug contains a polycyclic ring system (rings A-D), a glycosydic moiety at C1, and a pendant ring (E-ring) at C1. Etoposide inhibits the ability of topoisomerase II to relax DNA that it cleaves during the double-stranded DNA passage reaction. Consequently, drug treatment generates high levels of topoisomerase II-associated DNA breaks in cells, triggering apoptosis. Humans possess two topoisomerase II isoforms, α and β. Topoisomerase IIα is expressed in rapidly proliferating cells and is required for DNA replication and mitosis. Topoisomerase IIβ, is expressed in all cells irrespective of proliferative state. Despite the clinical importance of etoposide, little information exists regarding its interaction with topoisomerase IIβ.

Objective: To determine the substituents on etoposide that are important for its activity against topoisomerase IIα and to compare them with those that mediate drug interactions with topoisomerase IIβ.

Methods and Materials: Etoposide derivatives with modifications at the A-ring, E-ring, and glycosydic moiety were examined for their effects on DNA cleavage (global and site-specific) and religation mediated by topoisomerase IIα and β.

Results: Modifications of the A- and E-rings dramatically reduced etoposide activity, while alterations of the glycosydic moiety had little effect. None of the changes altered drug effects on the DNA cleavage specificity of topoisomerase IIβ.

Conclusions: Results demonstrate that the A- and E-rings of etoposide are important for drug activity against topoisomerase IIβ, while the glycosydic moiety is not. None of the alterations affected enzyme-DNA interactions. Findings correlate with those seen for topoisomerase IIα.

Acknowledgements: Ryan P. Bender, Jo Ann Byl and Neil Osheroff, Vanderbilt University School of Medicine.

Localzation of Retinoic Acid Synthesis and Signaling in Hair Follicle Morphogenesis

Naomi Yoo
Laboratory-Based Research

Background/Problem: Retinoic acid (RA) is necessary for the development and differentiation of many organ systems including the skin and hair follicle. Previously we demonstrated that components of RA synthesis and signaling localized to specific structures in the adult cycling hair follicle, which may regulate its cycling. Objectives: Our aim is to better understand the role of RA in hair follicle development by localizing the components of RA synthesis and signaling during follicle morphogenesis.

Methods and Materials: Based on studies in the mature hair cycle we chose 5 of the 9 components of RA synthesis and signaling to study. Immunohistochemistry was performed on dorsal skin from 0-10 day old C57BL/6j mice using antibodies against retinol dehydrogenase (Drh0), retinal dehydrogenase (Alldh1a2, Alldh1a3), cellular retinoic acid binding protein 2 (Crabp2), and retinoic acid receptor alpha(Rara) to study the eight stages of follicle morphogenesis.

Results: All components sufficient for retinoic acid synthesis were found in the precortex area when differentiation into various layers begins early in development using Alldh1a3 and in the bulge later in morphogenesis using Alldh1a2. The sebaceous gland likewise contains all components of retinoic acid synthesis, with RA synthesis enzymes localizing the less differentiated cells and RA signaling proteins localizing to the nucleus of more differentiated sebocytes. In addition, Alldh1a2 and Alldh1a3, although similar in function, uniquely localized to the epidermal plug and bulge versus the companion layer, precortex, inner root sheath, and dermal papilla respectively.

Conclusions: These data suggest that RA synthesis and signaling may regulate growth and differentiation of all layers of the hair follicle during morphogenesis.

References: Available upon request.

An In Vitro Study of a Potential Angiostatic Mechanism of Anecortave Acetate

Michael Young
Laboratory-Based Research

Background/Problem: Anecortave acetate, an angiostatic steroid, has been shown to inhibit angiogenesis in several different animal models. A previous in vivo study shows that anecortave acetate may upregulate expression of an endogenous proteinase inhibitor, plasminogen activator inhibitor type-1 (PAI-1). This inhibitor may play a role in angiogenesis.

Methods and Materials: We have designed and performed experiments to test the hypothesis that anecortave acetate induces PAI-1 expression through increased transcription of the PAI-1 gene.

Results: Anecortave acetate increased PAI-1 mRNA expression peaking at two hours post-treatment and PAI-1 protein levels were highest at 24 hours post-treatment. Anecortave acetate increased PAI-1 promoter activity in HREMC transfected with a PAI-1 promoter-luciferase reporter construct.

Conclusions: These results indicate that anecortave acetate increases PAI-1 levels by increased PAI-1 gene expression. Inhibition of the proteolytic aspect of the angiogenic cascade mediated by PAI-1 up-regulation is of potential therapeutic value in angiogenic conditions such as diabetic retinopathy and age-related macular degeneration.


Acknowledgements: John S. Penn, PhD, Gary McCollum, PhD, Joshua Barnett and Rong Yang, Vanderbilt Department of Ophthalmology and Visual Sciences.
Law and 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 interdisciplinary course with law and divinity students explored the intersections of 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.

Some of the students went on to propose and even implement policy reforms. One preformed a comprehensive analysis of existing laws and pending legislation across the country in an area of major interest to Vanderbilt in the Tennessee legislature. One worked for a Congressman who is a leader in health care policy and this student is now playing a major role in redesigning components of the undergraduate medical school curriculum. Another worked for the Institute of Medicine on a project to increase the supply of organs for transplantation, thus gaining an insider’s view on that issue. Another student assisted lawyers who were actively litigating in the Tennessee legislature. One worked for a Congressman who is a leader in health care policy and this student assisted lawyers who were actively litigating in the Tennessee legislature. One worked for a Congressman who is a leader in health care policy and this student assisted lawyers who were actively litigating in the Tennessee legislature.

Allen Clayton, M.D., J.D., holds the Rosalind E. Franklin Chair in Genetics and Health Policy at Vanderbilt University Center and is the Co-Director of the Center for Biomedical Ethics and Society. She joined the Vanderbilt faculty in 1988 and holds appointments in both the Medical School and Law School. Dr. Clayton is one of the preeminent scholars in the field of law and genetics. She has numerous publications in books, medical journals, interdisciplinary journals, and law journals on the intersection of medicine, law, and public health. In addition to teaching in the Law School and Medical School, she is a practicing pediatrician at the Vanderbilt Medical Center.

Evaluation of Tennessee Providers Over-Prescribing Narcotics and TDOH Response

Jordan Yockey
Law and Policy

The study evaluates the prescribing habits of the past year for Schedule II narcotics in Tennessee of the top three hundred prescribers, made up of two groups—those who received letters from the Tennessee Department of Health (TDOH) concerning their prescribing habits (n = 35), and a control group consisting of the remainder in the upper 1% (n = 140) who did not receive a letter from TDOH. Individuals under investigation by state or federal government for prescribing habits and provider groups (hospitals, clinics, etc.) in the top 1% were eliminated from the study, as the were not sent letters by TDOH.

To evaluate the effectiveness of these letters in reducing scripts written for narcotics, comparison of the average number of scripts written for the two month prior to and two months after the letter were made for those in the control group and those who received the letter for the first time (in a 4:1 random sample). These two monthly figures were averaged. A difference was found between the average number of prescriptions before and after the letter. In addition, the number of physicians whose scripts decreased from pre- to post-intervention were identified for comparison.

Results:
Average scripts written increased after the intervention in both the group who received letters and the control group for the same time period, although the TDOH letter group increased slightly less (3 scripts versus 9 scripts from pre- to post-letter). The TDOH letter group had 16 providers (45.71%) decrease scripts after receiving the letter in comparison to the 45 providers (32.14%) who decreased in the control group.

Conclusions:
The letters sent to top prescribers had only a slight impact on those providers. It limited their increase over the time period from pre-intervention to post intervention by six scripts on average (increase of 3 as compared to 9 scripts for the letter group and the control group). If both groups had been equally impacted, the TDOH letter group would have shown an increase of 13% (8 scripts versus 9 scripts from pre- to post-letter). The TDOH letter group was expected to be more effective in curbing high prescribers. This study suggests that further evaluation needs to be conducted in order to find a way to better identify top prescribers and find another intervention alternative with a more successful outcome.

Acknowledgements:
Dr. Larry Arnold and Robbie Bell, Tennessee Department of Health, Dr. Ellen Wright Clayton, Joshua Perry, Dr. William Cooper, Dr. Bruce Schaffner and Dr. Anderson Spickard, Vanderbilt University Medical Center.
Medical Humanities

The area of Medical Humanities encompasses a wide array of disciplines, each with its own literature, methods and issues. What these disciplines have in common is the focus on human experience and an examination of human values. The core activity of the medical humanities is critical reading and interpretation of texts that speak to central issues. What these disciplines have in common is the focus on human experience and an examination of human values. The core activity of the medical humanities is critical reading and interpretation of texts that speak to central issues.

Mark Bliton, Ph.D., is an Associate Professor in the Department of Medicine, with secondary appointments in the Department of Obstetrics and Gynecology and the Department of Philosophy at Vanderbilt University. He serves as the Chief of Vanderbilt University Medical Center’s Clinical Ethics Consultation Service. He is also the Area Director for Medical Humanities in the Emphasis Program at Vanderbilt’s School of Medicine. Within the Center for Biomedical Ethics and Society, Dr. Bliton is the primary supervisor for students from Philosophy, Religion, Divinity, and other main campus programs interested in pursuing clinical ethics activities and experiences.

“A hallmark of my experience with the students in the Humanities area was the diversity of the interests they embraced. Combined with the energy and focus they applied to their projects, that range of interests presents the initial strength of the Emphasis Program as these students grow to meet the dual challenges of a dynamic and increasingly stratified health care system.”

A Comparison of Women Undergoing Breast Augmentation and Tissue Expander-Implant Reconstruction

Megan Herceg
Medical Humanities

Background/Problem: In 2005 there were nearly 300,000 breast augmentations and 60,000 breast reconstructions performed in the United States. Breast augmentation was the third most frequently performed cosmetic surgery, accounting for 16% of all cosmetic procedures, while breast reconstruction accounted for 1% of all reconstructive surgeries. To date there is little, if any, literature directly comparing these two procedures.

Objectives: This study looked at women undergoing elective breast augmentation and tissue expander-implant breast reconstructive surgery. The objective of the study was to assess women’s goals and motivations for seeking surgery, and their satisfaction with the procedures. Patients’ narratives on body image, perception of the breast, femininity and self-identity were also collected and analyzed to understand the personal and social relevance of reconstructing the breast.

Methods and Materials: The study adopted a qualitative, narrative methodology. The author created an ad hoc semi-structured schedule for pre-operative and post-operative interviews with patients and conducted participant observation in the Plastic and Cosmetic Surgery Clinics at VUMC. Two interviews were completed, one from each surgical group, and a comparative analysis of the patients’ responses was carried out using domain analysis to identify significant themes. The four domains analyzed were: procedural, body image, breast perception, and self-identity.

Results: Both women cited the opportunity to regain a sense of “normality” as a motivation for surgery. Carrie (pseudonym), the breast augmentation patient, reported being satisfied with her body, but unhappy with her current breast size. She also identified the breast as the defining symbol of being a woman. This was not the case with Susan (pseudonym), the reconstructive surgery patient, who was older and happy with both her body and the size of her breasts. She did not identify any one characteristic as a marker of womanhood.

Conclusions: Despite different circumstances surrounding these two types of breast surgery, re-establishing a sense of normality emerged as an important priority in both groups. A closer analysis of patients’ motivations, goals, satisfaction, body image, breast perception, femininity and self-identity can help physicians to understand variable standards of normality for patients undergoing breast surgery.


Acknowledgments: Special thanks to the women who participated in this study as well as the nursing staff in the VUMC Plastic and Cosmetic Surgery Clinics for their help. In addition, Dr. Lucia Tanassi, Assistant Professor of Medical Ethics and Anthropology, Center for Biomedical Ethics and Society, Vanderbilt Medical Center and Dr. R. Bruce Shack, Professor and Chair of Plastic Surgery, Department of Plastic Surgery, Vanderbilt Medical Center.

Three Treatments of Depression: Gaining Insight into the Future of Deep Brain Stimulation

Jim D. Phillips
Medical Humanities

Background: Deep brain stimulation (DBS) is rapidly expanding in medical significance. Initially limited to symptom control in advance staged Parkinson’s Disease, its use is now being explored for treatment in an array of psychiatric disorders, most prominently severe depression. As medicine steps into this new frontier of neural intervention, the literature is devoid of perspectives into how society will integrate this invasive and highly technical treatment modality into its collective consciousness. Speculation regarding this may be informed by examining how previous analogous treatments of depression fared in their medicalization.

Objectives: To illuminate some of the potential pitfalls that must be considered as DBS integrates itself more permanently into our culture as a viable treatment of depression by exploring the histories and controversies associated with electroconvulsive therapy (ECT).
and fluoxetine (Prozac®), two effective treatments for depression with nearly polar opposite social understandings.

Methods and Materials: This study was conducted by examining relevant literature in peer review journals and published books as well as by interviewing experts in neuroscience, neuropsychology, psychiatry, and biomedical ethics at Vanderbilt University. In light of the information gathered, preliminary writings became the building blocks for a final paper.

Results: Beyond learning the fascinating histories of the developments of ECT, Prozac, and DBS, I have most significantly discovered that marketing (or lack thereof) has played, in many ways, the greatest role in keeping ECT from being more widely used but allowing Prozac to not only become ubiquitous as a treatment option, but to transform the very formulation of depression as a disease concept. While DBS shares a number of physical properties with ECT, parallels in its development can be drawn with that of Prozac, suggesting that it will more likely follow a similar path in its acceptance.

Conclusions: DBS is at a crossroads in its history as its proven application in late stage Parkinson’s disease gives way not only to possible use for stemming disease progression in early Parkinson’s Disease, but to use for treating a bevy of psychiatric ailments. These range from obsessive compulsive disorder to Tourette’s Syndrome to major depression. Given how the social acceptability of previous innovative treatment modalities for depression depended as much upon scientific demonstration of safety and effectiveness as on skilled marketing and persuasion of both patients (viewed as consumers) and those in the medical community, it is not unreasonable to imagine that marketing efforts will likely also play a major role in establishing DBS as a viable treatment (given minimal demonstration of safety, tolerability, and effectiveness) in the setting of depression.

References: Complete list of references available upon request.

Acknowledgements: Stuart Finder, PhD, The Center for Biomedical Ethics and Society, David Charles, MD, Neurology, Joseph Neimat, MD, Neurosurgery, and Stephan Heckers, MD, Psychiatry, Vanderbilt University Medical Center; and Jeff Schull, PhD, Psychology, Vanderbilt University.

Conclusions: A “Two-Viewpoint” Approach to Disease, Free Will and Responsibility: Implications for Clinicians

Brent R. Taylor
Medical Humanities

Background: “Free will” is an individual’s capacity to choose a course of action independent of factors over which he or she has no control. Alternatively, “determinism” is the philosophical position that all events, even human choices, occur as the result of processes already in motion. Determinism has gained strength in the form of scientific materialism, which holds that scientific methodologies explaining human behavior in terms of testable genetic and environmental factors are capable of providing a comprehensive account of human action.

Objectives: This essay discusses how scientific materialism’s implications for free will and personal responsibility have created confusion in the medical and legal fields and suggests how belief in free will in the age of genetics can be reasonable. Issues analyzed include the accessibility of a given question to scientific inquiry, the meaning of causality and chance, and model construction in relation to axiom choice.

Methods and Materials: A literature review of PubMed articles under the search-term “free will” was conducted. As questions arose, select pertinent resources were consulted yielding a synthesis of arguments from the medical literature and from the fields of linguistic theory, literary analysis, historiography and philosophy of science.

Results and Conclusions: The preservation of belief in free will and personal responsibility is argued to be necessary for the maintenance of a sound understanding of the self and for an understanding of existence as personally meaningful. A “two-viewpoint” approach that acknowledges both free will and genetic and environmental constraints is proposed as an alternative to scientific materialism.

Acknowledgements: Many thanks to Dr. Larry R. Churchill, Professor of Medical Ethics, Vanderbilt University Medical Center, for his guidance and generosity in assisting with the development of this work.

“O Work Divine!”
Sir Kenelm Digby’s Study of Poetry and Embryology

Kim Lori Sandler
Medical Humanities

Background: Today there is a great divide between the sciences and the humanities. This schism did not always exist, however. In the Renaissance, an educated person was a virtuoso, well studied in a multitude of different fields. Sir Kenelm Digby, who proposed the modern model of conception known as epigenesis in 1641, was a poet, mathematician, and literary critic as well as a pioneer in the field that would become embryology. His embryological research was conducted on chick embryos, even though the microscope had not yet been invented. How did Digby theorize and explicate the science of conception without ever observing embryonic development at a microscopic level?

Objectives: To illustrate direct parallels between Digby’s embryological research and his analysis of poetry and to determine the influence of each on the other.

Methods and Materials: This paper examines two of Digby’s publications, his embryological work Two Treatises and an essay on Edmund Spenser’s Faerie Queene, with some consideration of two of Digby’s original poems. Its method of close reading is an established approach in the field of literary criticism for interpretation of text at its most detailed level. The paper also incorporates both biographical and historical information in order to provide context for Digby’s writings.

Results: An analysis of Digby’s writings suggests that he drew insights from several fields, particularly poetry, to theorize epigenesis before conducting any experiments.

Conclusions: Without his knowledge of poetry, philosophy, and other arts, Digby would not have conceptualized epigenesis. His education in humanities made up for the technology that was not yet available.

Acknowledgements: Advisor Jay Clayton and special thanks to Holly Tucker.
Medical Scientist Training Program

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 approximately 10 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.

Terence S. Dermody, MD, Professor of Pediatrics and Microbiology and Immunology, and Director of the Elizabeth B. Lamb Center for Pediatric Research, serves as Director of the Vanderbilt MSTP. Dr. Dermody came to Vanderbilt in 1990 after completing a residency in internal medicine at Presbyterian Hospital in New York and fellowships in infectious diseases and virology at Brigham and Women’s Hospital and Harvard Medical School in Boston. Dr. Dermody is a physician-scientist with clinical interests in pediatric infectious diseases and research interests in viral pathogenesis.

The Emphasis Program allows our MSTP students to complete three laboratory rotations and choose a mentor to guide the PhD thesis research. This is an incredibly important experience for our students. They gain exposure to a wide variety of research opportunities and select a mentor, training environment, and scientific project best suited to their professional development.”

Classification of Embryonic Toxicity of Sodium Channel-Blocking Local Anesthetics in Zebrafish

Jeff Bennett
Medical Scientist Training Program

Background: The external fertilization, optical transparency and rapid development make the zebrafish and excellent model to study heart development. In the zebrafish, circulation is established approximately 26 hours after fertilization. Though voltage-gated sodium channels are critical for action potential generation in the adult zebrafish heart, administration of the sodium channel antagonist tetrodotoxin recently showed that the channels are not required for circulation until day 4.5. Before this time, tetrodotoxin has no effect on heart rate, suggesting an alternative mechanism of depolarization before then. Nonetheless, after subjecting zebrafish embryos to the sodium channel antagonists tricaine and lidocaine, developmental defects were discovered. Lidocaine disrupted epiboly of the animal pole, while tricaine, a similar drug, prevented midline fusion of cardiogenic progenitor cells, resulting in cardiac bifida.

Methods and Materials: Based on these observations, we hypothesize that sodium channels have a function in the developing embryo, independent of their activity as voltage-gated channels. We will attempt to phenocopy the observed effects of local anesthetics with the more specific antagonist TTX, and structurally similar local anesthetics. The expression levels of both early (Nkx2.5, Gata4) and late (CMLC2, LTCC) genetic markers of cardiac lineage will be assessed by real-time quantitative PCR. The sodium channel agonist ATX II will be used to attempt to rescue the phenotype.

Future Directions: We hope to find a critical development window in which voltage-gated sodium channels play non-depolarizing role in the zebrafish embryo and establish local anesthetics as tools to understand the critical developmental processes of gastrulation and epiboly.

Acknowledgements: Co-authors: Sameer Chopra, Tao Zhong, and Dan Roden.

Planning Needle Placement in Image-Guided Radiofrequency Ablation of Hepatic Tumors

Chun-Cheng Richard Chen
Medical Scientist Training Program

Overview/Background: In hepatic applications, successful treatment with radiofrequency ablation (RFA) requires proper placement of the device so that the resulting ablation extents overlap the detectable tumor as well as a suitably defined margin. Current methods of treatment planning, however, use geometric models of ablations that are independent of the actual physical processes governing RFA, thus incorrectly predicting final ablation outcomes.

Objectives: This research examined novel methods to develop optimal needle placement treatment plans using predictive computational modeling and characterized the efficacy of the plans when implemented using image-guided techniques.

Methods and Materials: A search method using finite element models of RFA was created to obtain needle placements that optimized a given therapeutic goal. A phantom system was then constructed to compare ablation experiments performed using a tracked RFA device with model predicted outcomes. Finally, the sensitivity of predicted ablations to needle placement inaccuracies was studied theoretically by coupling boundary element and finite element methods together with a Monte Carlo scheme to generate a probability map of ablation success given uncertainties in needle placement.

Results and Conclusions: When applied to simulated scenarios, the planning system was able to optimize placement of the RFA needle in the presence of nearby vessels. These treatment plans also used fewer ablations than geometric plans. Computational models, based on positional data of the device during phantom ablation, also agreed with 90% of the resulting imaged ablation extents. Sensitivity analysis using the boundary method showed the utility of multiple ablations in producing treatments that were less sensitive to placement errors. The results of this research demonstrated the feasibility of using image-guided techniques along with computational models to deliver robust and predictive RFA treatments.

Acknowledgements: This research was supervised by Dr. Bob Galloway and Dr. Michael Miga.
The Impact of Bacterial Infection on The Activity of NKT Cells
Curts Lee Gabriel
Medical Scientist Training Program

Overview/Background:
Classical NKT cells are a lymphocyte subset with an invariant T cell receptor (TCR) restricted to lipids presented by CD1d, a member of the major histocompatibility complex family. NKT cells are able to modulate the immune response in various diseases. Infection with pathogens such as E. coli or Shigella may affect the activity of NKT cells, leading to exacerbation of various diseases. Several pathogens have already been examined by the Van Kaer lab. I hope to expand the list of pathogens studied when I begin my thesis work.

Objectives:
To determine the impact of E. coli infection on the activity of NKT cells in mice.

Methods and Materials:
Mice were injected with heat-killed E. coli. After four weeks, splenic lymphocytes were harvested from the mice. The lymphocytes were then challenged in vitro with -galactosylceramide (-GalCer), a glycolipid that activates NKT cells. NKT cell proliferation was measured via radioactive labeling and cytokine secretion was measured with ELISA.

Results:
NKT cells harvested from mice challenged with heat-inactivated E. coli were less responsive to -GalCer stimulation than control mice, as measured by proliferation and cytokine secretion.

Conclusions/Future Directions: Injection of heat-killed E. coli causes NKT cell anergy in mice. This phenomenon may play a role in disease exacerbation, and will be examined in the context of animal models of multiple sclerosis, asthma, and other diseases. We will also examine NKT cell activity in models of other infectious diseases, including Listeria.

A Novel Role for p120 in the Nucleus
Nick Markham
Medical Scientist Training Program

Background:

Methodology:
We performed a flow cytometry-based FRET assay to examine subunit adjacency. For p120 receptors, FRET was observed not only between p12- and β2 subunits, but also between β2 and γ2 subunits and, to a lesser extent, between α1 subunits. Addition of the γ2 subunit substantially decreased FRET between α1 and β2 subunits and nearly eliminated FRET between p120 and β2 subunits. For efficient expression of subunit combinations, p120-catenin activity is negatively regulated by interaction with CtBP1, a nuclear binding protein 1 (CtBP1). Immunofluorescence and molecular experiments confirm a physical interaction between p120 and Glis2 and show co-localization in the nucleus under some circumstances. p120 appears to promote the cleavage of Glis2 and stabilizes the cleavage product, but does not affect Glis2’s DNA-binding properties.

Acknowledgements:
Botzolakis EJ, Stanley AK, Lagrange AH, Lo W and Macdonald RL.

A Novel Role for p120 in the Nucleus
Results: Preliminary analyses show that association to a region in intron 3 of the GABRB3 gene is replicated in a much larger set of families than previously assessed by McCauley et al. Since the associated SNPs appear to span more than 1 block of LD, this may be evidence of multiple risk alleles within the GABRB3 locus which may predispose individuals to autism.

Conclusions: The focus of SNPs in intron 3, especially the associated blocks near exon 4 and exons 1-3, makes these very appealing targets for further study. Sequencing of families linked at the GABRB3 locus is presently underway. Meanwhile, we intend to further explore the regions showing single-marker or haplotype association to further elucidate the elements which may be driving the signal detected.

References:

Methods and Materials: SAD: Mice were anesthetized with 1-4% isoflurane and placed supine on an Isothermal pad. A ventral midline incision was made in the neck, exposing the carotid bifurcation. The superior cervical ganglion and superior laryngeal nerves were isolated and removed. The adventitia and associated connective tissue were stripped from the carotid sinus region. BP was measured via intraarterial catheter and HR was monitored by 2-lead ECG, both connected to Gould amplifiers and a WinDag data acquisition system. Gastrostomy: An upper abdominal midline incision was made to expose the stomach. The corpus was punctured at the greater curvature with blunt forceps and purse-string sutures were placed in the seromuscular layer surrounding the opening. A PE-50 catheter was inserted into the gastric lumen just beyond its fabricated blunted and flanged end and the sutures were tightened and tied to form a secure seal. Fluids were infused into the stomach at a volume of 750ml per 25g body weight (BW) over 3 min.

Results: We observed a change in systolic blood pressure (SBP) of 13.9 ± 0.1 mmHg appearing 3 minutes after water infusions and peaking at 15-20 minutes. Infusion of an identical volume of physiological saline showed a decrease in SBP of 7.5 ± 0.2 mmHg (p<0.001). The effect in patients appeared 5-10 minutes after water ingestion and was maximal between 25-40 minutes. In contrast, young subjects with normal functional autonomic systems showed no noticeable pressor response after water ingestion. In non-SAD mice, infusion of water resulted in an immediate pressor response different in nature than that observed in SAD mice and in patients with dysautonomia. The increase in SBP observed in non-SAD mice occurred over a significantly shorter time course, with SBP returning to baseline 12 minutes post infusion. The effects observed after water infusion in SAD and non-SAD mouse models match well with those observed in dysautonomic patients and normal subjects, respectively, with the gastropressor effect only in cases where the autonomic nervous system has been impaired.

Conclusions: The SAD mouse model may prove useful in elucidating the mechanism of the gastropressor response.

Acknowledgements: N.R. Keller, M. Appalsamy, A. Sutcliffe, J. Jordan,  Franz-Volhard Clinical Research Center, Berlin, Germany. The Role of Neurosubstrates in Differential Processing of Multisensory Reading Cues

AI Powers Medical Scientist Training Program

Background: Developmental dyslexia, characterized by persistent reading difficulties in childhood, has been assigned several root causes, the most prominent of which are high-level phonological processing deficits and impaired single-sense visual or auditory processing. Objectives: We propose that dyslexia may also be caused by deficits in the integration of multisensory information. Recent studies by our laboratory suggest that...
Additionally, the role of VEGF-A in pancreatic islet vascularization and an essential angiogenic factor for normal (VEGF-A) has been identified as an

Background:

Innervation

VEGF-A in Islet

Elucidating the Role of

VEGF-A in Islet Innervation

Rachel Reinert

Medical Scientist Training Program

Background:
The incidence of diabetes is rapidly increasing in the United States, yet the mechanisms underlying its pathogenesis remain unclear. Recently, the vascular endothelial growth factor A (VEGF-A) has been identified as an essential angiogenic factor for normal pancreatic islet vascularization and function (Brissova et al., 2006). Additionally, the role of VEGF-A in modulating the synchronous development of peripheral nerves and blood vessels has been described (Mukouyama et al., 2002 and Carmeliet and Tessier-Lavigne, 2005). While pancreatic islets are well innervated by sympathetic, parasympathetic and sensory nerve fibers, molecular factors and mechanisms responsible for this cellular organization are incompletely defined.

Objectives:

We hypothesize that VEGF-A, in addition to being required for the development of islet vasculature, is also important in directing and maintaining islet innervation.

Methods and Materials:

First, the innervation of wild-type mouse islets will be visualized at embryonic, neonatal and adult stages using immunohistochemistry and fluorescence microscopy. Next, the role of VEGF-A in islet innervation will be studied using a Cre-loxP strategy, allowing for the spatial and temporal control of VEGF-A gene inactivation. The impact of VEGF-A on islet innervation will be studied in mice that lack VEGF-A throughout the pancreas (Pdx-1-Cre; VEGF-loxP) or specifically in beta cells (Rip-Cre; VEGF-loxP). In addition, a tamoxifen-inducible Cre-loxP system (Pdx-1-IB-CreER; VEGF-loxP) will allow us to study the effect of VEGF-A reduction on islet innervation in adult pancreatic islets.

Results:

Preliminary data show that the number of Schwann cells is increased in Pdx-1-Cre; VEGF-loxP mice compared to wild-type controls. Schwann cell proliferation is reduced by 50% in the absence of VEGF-A. The number and area of visible blood vessels is reduced in the absence of VEGF-A. These data suggest a role for VEGF-A in the development and maintenance of islet innervation.

Conclusions:

While VEGF-A is essential for normal islet innervation, the precise mechanisms by which it regulates this process remain to be elucidated. Further studies are needed to determine the role of VEGF-A in the development and maintenance of islet innervation.

Acknowledgements:

Mary M. Zutter, MD, Vanderbilt University School of Medicine.

Expression and Purification of Human Rotavirus-Specific Monoclonal Antibodies

Fyza Shaikh

Medical Scientist Training Program

Background/Problem:

Rotavirus, a non-enveloped RNA virus, is the most common cause of severe diarrhea, hospitalizations and death among children worldwide. The majority (85%) of deaths due to severe dehydration, resulting from rotavirus infection occur in the developing world, citing a critical need for effective vaccines in areas with limited health services. However, a lack of knowledge on the mechanisms behind the immunity of the infant antibody response to viral pathogens, including structural determinants, binding sites, and the role of somatic mutations, makes a clear correlation between high affinity antibodies and functionality (such as neutralization) difficult. Currently known antibodies for rotavirus have different specificities for viral particles, which may affect how the virus is treated by the immune system. One of these anti-bodies, RV6-26, was characterized previously by expression in bacterial HB2151 cells, purification, and binding (BioCore) assays to antigens or cells infected with rotavirus. Two other antibodies in the VH4-31 and VH4-61 families were characterized initially but studies were incomplete.

Methods and Materials:

RV6-26, RV6-48, RV6-65, and RSV Fab19 were expressed in non-suppressor E. coli HB2151 and extracted from the periplasmic space using toll different buffers: TES buffer and B-PER cell lysis buffer. Fab were then purified using a Ni+ column and run on 12% SDS-PAGE gels.

Results:

Fab was present in TES extract and combined fractions of Fab19 and 6-26 but not 6-48 and 6-65. Fab were present in the PER extract for Fab19, 6-26, and 6-65. PER Fab peaks for Fab19, 6-26, and 6-65 in fraction 3. Fab production was not detected for 6-48 in either buffer.

Conclusions:

Although the TES extracts did not show a UV peak for any sample during purification with a Ni+ column, Western blot analysis did show presence of Fab in combined fractions for Fab19 and 6-26. During purification of PER fractions, a UV peak for Fab19, 6-26, and 6-65 was seen and the presence of Fab was confirmed by Western analysis. Expression of 6-48 Fab was not seen in either TES or PER, indicating a need for optimizing expression vector, culture conditions, and/or extraction.

Acknowledgements:

Mentor James E. Crowe, Cuixia Tran, Nicole Kallewaard, Frances House and other members of the Crowe lab, Vanderbilt University Medical Center.

Role of α2β1 Integrin on Cell Dysplasia and Carcinogenesis in K14-HPV16 Transgenic Mice

Thuy T. Tran

Medical Scientist Training Program

Background/Problem:

The α2β1 integrin mediates adhesion to collagen and laminins and is expressed on a number of cell types including epithelial and endothelial cells. It is known that proliferating epithelial cells up-regulate expression of α2β1 integrin.

Objectives:

As a model of squamous carcinogenesis, transgenic mice expressing HPV16 early region genes (E6/E7) under control of the K14 promoter were used to study the impact of the α2β1 integrin on premalignant cellular transformation involved in squamous cell carcinoma.

Methods and Materials:

α2β1-null mice were backcrossed 8 generations into a FVB/n background and subsequently mated with K14-HPV16 transgenic mice, thereby producing either wild type (α2β1+/-) or α2β1 integrin-null (α2β1-/-) animals. All mice included in this study were noted for visible tumor development, with biopsies and monitoring of the mice also being required to validate and elaborate on these preliminary findings.

Future Directions:

More experiments will be needed to elucidate the mechanistic role of α2β1 integrin in cellular changes associated with carcinogenesis. Future experiments include blood and tumor sampling via FACS for determining inflammatory cell composition. More biopsies and monitoring of the mice will also be required to validate and elaborate on these preliminary findings.

Acknowledgements:

Andrea M. Sheehan, MD, Laura E. Wells, Lisa M. Coussens, PhD, and Mary M. Zutter, MD, Vanderbilt University School of Medicine.
Patient-Oriented Research

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, developmental, 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 area is the scientific study of 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 area 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 lifelong learner, effective problem-solver, and compassionate thinker. To paraphrase William Osler, ‘No matter how trifling the clinical question on hand, answer it with a feeling that it demands the best that is in you, and when done look it over with a critical eye, not sparing a strict judgment of yourself.’ Through the auspices of the Emphasis Program, I wish to inculcate such a spirit of reflection in each medical student.”

Jayant Shenai, MD, is the Director of Educational Affairs for the Division of Neonatology, Vanderbilt Children’s Hospital. He is responsible for coordinating the education of neonatologists, community physicians, neonatology fellows, pediatric residents, nurses, and others in healthcare. His primary research interests include vitamin A in relation to chronic lung disease in pre-term infants and related clinical applications. As the Editor-in-Chief of NeoReviews Plus, he contributes to the Self-Assessment Program for neonatologists developed by the American Academy of Pediatrics. He has spoken by invitation in Europe, the Middle East, Canada, and Mexico. He participates in the grant review process at the National Institutes of Health as a member of the Study Section of Reproductive Biology. He is an Amos Christie Award winner for his outstanding teaching accomplishments and was a 2006 recipient of an Excellence in Teaching award for his contribution to continuing medical education.

Vivek Agarwal
Patient-Oriented Research

Background:
In the United States, there are 55,000 patients cared for daily in over 6,000 ICUs. Patients above the age of 65 occupy more than 55% of these beds. The most common reason for ICU admission is respiratory failure and the need for mechanical ventilation. Recent studies indicate that non-pulmonary acute organ dysfunction may contribute significantly to mortality and other important clinical outcomes. Delirium occurs in 10-60% of the older hospitalized population, yet often goes unrecognized by the medical team. Delirium is an important independent prognostic determinant of hospital outcomes including nursing home placement, functional decline and death.

Objectives:
Evaluate the prevalence of delirium in Burn ICU patients in addition to its risk factors and the outcomes associated with development of delirium.

Methods and Materials:
This observational study is conducted with IRB approval with waiver of consent. 150 consecutive adult Burn ICU patients who require mechanical ventilation for more than 24 hours are assessed for delirium using the Richmond Agitation Sedation Scale and Confusion Assessment Method for the ICU.

Results:
This study is currently ongoing and to date 75 patients have been enrolled.

Conclusions:
This study will provide data on an understudied population and lead to more goal directed sedative regimens in the ICU that lessen the prevalence of delirium, a significant contributor to poor clinical outcomes.

References:

Acknowledgments:
Dr. Pratik Pandharipande and Dr. Wes Ely, Vanderbilt University Medical Center.

Improving Diabetic Foot Screening Rates in an Academic Primary Care Clinic

Charlotte Brown
Patient-Oriented Research

Background:
The diabetic foot exam (DFE) is an important, recommended component of preventive care for patients with diabetes. Current recommendations are that the DFE should be performed annually for every patient with diabetes. However, the rate yearly DFE is variable among primary care providers. Our objectives were to measure our rate of DFE performance on patients with diabetes and to use quality improvement interventions to improve compliance with DFE performance and documentation.

Methods and Materials:
The diabetic foot exam (DFE) is an important, recommended component of preventive care for patients with diabetes. Current recommendations are that the DFE should be performed annually for every patient with diabetes. However, the rate yearly DFE is variable among primary care providers. Our objectives were to measure our rate of DFE performance on patients with diabetes and to use quality improvement interventions to improve compliance with DFE performance and documentation.

Results:
We identified 337 patients who met the initial inclusion criteria. Our chart review revealed that our baseline rate of yearly four-component DFE was 17%. By the end of the twelve-month intervention period, the number of patients with diabetes who were cared for at our site had increased to 387. After implementation of the patient education posters the proportion of patients with a documented DFE increased minimally. In the first months that the EMR reminder was implemented, this intervention accounted for over half of the newly DFE. Use of the team approach initially yielded an additional 29% improvement in DFE completions and successfully overcame several identified barriers. The team DFE proved to be a very sustainable intervention and
Incidence of Deep Vein Thrombosis in Patients Receiving Mega Prosthesis Placement for Oncologic Indications

Jason A. Castellanos
Patient-Oriented Research

Background: Patients undergoing joint replacement of the hip or knee are at increased risk for the development of deep vein thrombosis. Chemical prophylaxis such as heparin and coumadin is often implemented to reduce this risk. In certain patient populations receiving Mega Prostheses, however, oncological therapies preclude this preventive measure.

Methods and Materials: Sixty-three patients who underwent hip, femur and tibia Mega Prosthesis placement at Vanderbilt University Medical Center over a seven year period were included in the study. All patients received postoperative enoxaparin, pneumatic compression and thromboembolic deterrent stockings. Two patients received additional preoperative prophylaxis with either coumadin or heparin.

Results: Out of sixty-three patients, three patients had deep vein thrombosis and one patient developed a subclavian vein thrombosis associated with an infected Port-a-Cath. Of these patients with deep vein thrombosis, two underwent distal femur reconstruction and one underwent proximal femur reconstruction. The prevalence of deep vein thrombosis was higher following replacements in patients with sarcoma (2 of 24) than after replacements in patients with carcinoma (1 of 15) or hematologic malignant disease (0 of 2). Wound complications occurred in 4 of 24 patients with sarcoma, 1 of 15 with carcinoma, and 2 of 2 patients with hematologic malignant disease. Data analysis is incomplete at this stage.

Conclusions: The rate of deep vein thrombosis in patients who underwent Mega Prosthesis replacement of tibia, femur and hip was low with the use of postoperative pneumatic compression, thromboembolic deterrent stockings and enoxaparin despite the lack of preoperative chemical prophylaxis.

Acknowledgements: Ginger E. Holt, MD, Department of Orthopaedics, Vanderbilt University Medical Center.

Cost-Effectiveness of the Hybrid OR for Patients Undergoing Coronary Artery Bypass Grafting

Jonathan Chrispin
Patient-Oriented Research

Background: Following coronary artery bypass surgery (CABG), angiography is not immediately performed to test the success of the procedure. The hybrid OR was established to allow intra-operative assessment of the graft through angiography to determine whether further surgical repair or percutaneous intervention (PCI) is necessary.

Methods and Materials: A database was established which contained every aspect of the cost of care for the specific visit in which a CABG or hybrid procedure was performed. The financial database was further broken down into three subgroups depending on whether a planned or ad hoc PCI was performed. Using the statistical analysis the cost to the hospital of those undergoing a Hybrid or CABG procedure was determined.

Results: Seventy-one patients who underwent CABG procedures and 144 patients who underwent Hybrid procedures were enrolled into the financial database. All three hybrid subgroups had a higher direct cost, indirect cost and hospital charges when compared to the CABG only group (p<0.01). Further, the significant difference was due to the cost of cardiac catheterization supplies (p<0.01).

Conclusions: The cost to perform a Hybrid procedure is significantly greater than performing the traditional CABG. We plan to create a one year follow-up database and determine any differences in morbidity and mortality as well as differences in additional medical cost within the year following a patient’s hybrid or CABG procedure.

Acknowledgements: Dr. John Byrne, Dr. David Zhao, Dr. Geoffrey Day, Mr. Thomas Ervin, Sam Crosby, Brad Corr and Kim Jiramongkolchua, Vanderbilt University Medical Center.

Ventricular Volume Associations with Transient Encephalopathy Following Deep Brain Stimulation Surgery

Andrew B. Conrad
Patient-Oriented Research

Background: High frequency stimulation of the subthalamic nucleus (STN) with surgically placed electrodes has proven an effective treatment option for advanced Parkinson’s Disease (PD) with exemplary short and long-term outcomes (Fria et al, 2006). Deep brain stimulation surgery interventions are reversible, adaptable to patient clinical status, and reduce the needs and costs of medication with stable results (Charles et al, 2004). Nevertheless, the proper selection of patients who will reliably benefit from this procedure currently lacks any standardized assessment protocols. Clinical predictive factors of outcomes have been tentatively identified but demand clarification and refinement as shown by the persistence of postoperative morbidity and prolonged recoveries (Weiler et al, 2002). Exploration of anatomical factors may reveal correlations with clinical predictive factors as well as independent indices of surgical results.

Methods and Materials: Records from 61 patients undergoing bilateral DBS-STN procedures at Vanderbilt University from January 2002 to July 2005 were reviewed. From these, six patients with complicated recoveries and six age-matched controls with overnight recovery were identified. A 3D mask of the lateral ventricles was constructed. The standard atlas template was registered and deformed to patient preoperative axial T1-weighted MRI images for quantification of patient LVV. The application of gray-matter voxel intensity thresholds to MRI images yielded voxel counts for patient LBV values. For valid inter-subject LVV comparison, LBV-LBV ratios and gender-normalized LVV were compared using SPSS statistical software.

Conclusions: Absolute LVV were significantly greater among complicated subjects than in the overnight recovery controls (complicated= 34.98cm3, control = 23.49cm3, p=0.015). This observation remained significant and independent of size-related neuroanatomical variance with differences found in inter-groups comparisons of LVV-LBV (complicated= 0.029, control= 0.019, p=0.015) and gender-normalized LVV (complicated= 35.08cm3, controls= 23.74cm3, p=0.026).

Conclusions: In a retrospective review, higher LVV and LBV-LBV were predictive of prolonged postoperative encephalopathy in patients undergoing STN-DBS for PD. Prospective studies with larger number of subjects are needed to confirm these observations.

Acknowledgements: Co-authors: Thomas L. Davis, MD, Peter E. Korndorf, MD, PhD, and Michael Gensheimer. Vanderbilt University Medical Center; Benoit Dawant, PhD, and Srivatsan Pallavaram, BS, Vanderbilt University.
Effects of Procedural Time Due to Cardiac Hybrid Approach

Bradley R. Corr
Patient Oriented Research

Background: The cardiac “hybrid” OR at VUMC enables patients undergoing a CABG procedure to undergo PCI simultaneously if necessary. The integration of existing technologies into a new procedure has the potential for a number of benefits to the patients and physicians.

Objectives: To evaluate the hypothesis that the “hybrid” approach will provide shorter time on aortic cross clamp and CPB.

Methods and Materials: All patients who underwent CABG surgery and completion angiography in the “hybrid” OR between 04/2005 and 04/2006 were reviewed. Patients who received CABG and PCI (hybrid group) were compared with those who only underwent CABG (non hybrid group).

Results: 188 patients were identified, 56 patients underwent CABG with PCI and 128 patients without PCI. The average OR, anesthesia, CPB, and aortic clamp time for the hybrid patients was 414, 442, 85, and 56 minutes respectively. The average OR, anesthesia, CPB, and aortic clamp time for the non hybrid patients was 392, 420, 97, and 67 minutes. This resulted in statistical P values of 0.069, 0.078, 0.070, and 0.042 respectively. The average days of hospitalization for hybrid patients was 10.13 and 8.53 for non hybrid patients with a P value of 0.064.

Conclusions: The hybrid procedure does not statistically lengthen the patient’s total time in the OR or the total time under anesthesia. The aortic clamp time of hybrid patients is statistically shortened by an average of 10.3 minutes. However, CPB time is not shown to be statistically different for hybrid patients. Hospital length of stay is similar between both groups.

Acknowledgments: Mentor: John Byrne, MD, as well as David Zhao, MD, Geoffrey Day, MD, Christopher Paris, MD, Julie Damp, MD, Samuel Crosby, and Jonathan Chrispin, Vanderbilt University Medical Center.

Bleeding Effects of the Hybrid Approach to Coronary Artery Revascularization

Samuel N. Crosby
Patient-Oriented Research

Background: Concomitant hybrid revascularization with PCI and CABG may reduce complication and improve long-term outcomes in coronary artery revascularization. However, there has been much concern about the possibility of increased bleeding complications in such procedures due to aggressive anti-platelet therapy necessary for PCI.

Objectives: To study factors related to bleeding and compare hybrid patients to those only receiving CABG procedures.

Methods and Materials: We retrospectively studied the postoperative bleeding labs of 184 patients, 56 of which had hybrid procedures and 128 of which had standard CABG. Patients undergoing the hybrid procedures (mean age: 64.6±13.54, M/F:43/13 females) had an average 1.77±11.11 grafts and 1.77±14.14 stents. The patients undergoing conventional CABG procedures (mean age: 62.63±9.00, M/F:98/30) had an average 2.6±0.08 grafts. These two groups were compared based on hematocrit (HCT), platelet count as well as transfusion of packed red blood cells (PRBC), platelets, fresh frozen plasma (FFP), and chest tube drainage (CTD).

Results: Pre-operative platelet and HCT counts were similar in both groups. Post-operative HCT and platelet count remained similar in hybrid versus standard groups. There were no significant differences in post-op transfusion with PRBC (3.41±0.49 versus 2.80±0.28 units, p=0.13), platelet (1.05±0.43 versus 1.60±0.36, p=0.19), or FFP (0.73±0.23 versus 0.43±0.15, p=0.14) in hybrid versus standard group. Total CTD was higher in hybrid versus standard group (2050.90±260.79 and 1535.78±102.90 ml respectively, p=0.014).

Conclusion: Concomitant hybrid revascularization did not pose significant risk for bleeding complication compared to standard CABG. Increase in chest tube drainage does not significantly affect blood transfusions, platelet or HCT counts.

Acknowledgements: Dr. John Byrne and Dr. David Zhao, Vanderbilt University Medical Center.

Examining the Effectiveness of Helmet Therapy in Treating Positional Plagiocephaly

Amy K. Fenoglio
Patient-Oriented Research

Background: Plagiocephaly is a non-synostotic condition characterized by flattening on one side of the skull. Since the early 1990s, when the American Academy of Pediatrics began urging parents to put infants to bed in a supine position to reduce the risk of sudden infant death syndrome (SIDS), positional plagiocephaly rates have been on the rise. Helmet therapy is one of several ways to correct for such a cranial deformity. However, the validity of employing orthotic treatment versus positional molding therapy continues to be a subject of debate among physicians, and many third-party insurance payers have therefore dropped coverage for cranial remodeling helmets. The difficulty in affording such expensive devices in the absence of insurance coverage could have negative implications on health outcomes of plagiocephaly patients. In order to more clearly establish helmet therapy as a cost effective measure of prevention, a national scale, the effectiveness of the cranial remodeling helmet in treating positional plagiocephaly requires further study on a local scale.

Objectives: To quantitatively and qualitatively examine the effectiveness of helmet therapy in successfully correcting plagiocephaly among Vanderbilt-referred patients.

Methods and Materials: This retrospective study was conducted among craniofacial patients from Monroe Carell Jr. Children’s Hospital and referring pediatricians. Surveys were sent to the parents/guardians of former pediatric patients, dating back to 1998, who were referred to Dr. Kelly for helmet therapy. Data was gathered regarding the use of conventional positioning versus helmet therapy, duration of malformation prior to helmet use, age at helmet therapy initiation, satisfaction with therapy outcome, and necessity for further surgery. Questions used a combination of written responses and a 10-point Likert response to assess the above information. In addition, written response surveys were sent to Dr. Kelly’s referring pediatricians regarding the percentage of patients corrected by positional molding alone, the percentage of patients referred for helmet therapy, and the duration of conventional positioning attempted prior to referral for helmet therapy.

Results: Patient data suggests that 69% (49/71) of former helmet therapy patients tried positional molding techniques (i.e., head wedge, back wedge, positioning on stomach, etc.) before resorting to a therapeutic helmet. Satisfaction with helmet therapy outcome, as determined by the guardians of former patients, can be seen in Table 1. Average duration of cranial deformity prior to helmet use and average age at helmet therapy initiation, both with respect to satisfaction rating, are indicated in Figures 1 and 2. Satisfaction ratings of 8 or greater had an average deformity duration of 3.36 months and an average age of 6.63 months at helmet therapy initiation. It was determined that 4% (3/73) of patients who used a cranial remodeling helmet required further cranial surgery.

Physician data revealed that an average of 81% of patients with positional molding problems of the skull can be corrected by repositioning alone, and an estimated 13% of patients are referred for helmet therapy. The trial period of conserved positioning before physicians refer the patient for helmet therapy is an estimated 4.33 months on average.

Table 1: Satisfaction Level of Child’s Response to Helmet Therapy

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<th>Percentage of Patients</th>
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Figure 1: Duration vs. Satisfaction

Figure 2: Age vs. Satisfaction
Using Actigraphy to Measure Sleep in Children with Autism

Dina Ghoneim
Patient-Oriented Research

Background:
Parental questionnaire indicates a greater prevalence and severity of sleep problems in children with autism (ASD). It is important to better understand and measure sleep pathology in children with autism since sleep problems may exacerbate symptoms and may influence effectiveness of daytime interventions. Polysomnography (PSG) has been used as the gold standard in measuring sleep. Unfortunately, it presents a variety of obstacles to its routine use in the population of interest. In contrast, actigraphy, which has the potential to be worn at home over a period of weeks with minimal intrusion, presents significant advantages over PSG when measuring sleep in children with autism.

Objectives:
To gain experience with actigraphy as a measure of the sleep/wake cycle in children with autism.

Methods and Materials:
Study participants were children between the ages of 4 and 10 who were diagnosed with ASD. Actigraphy recordings were obtained from each child for a period of 5 to 19 nights. At least two of those nights included 2 consecutive nights of simultaneous PSG measurements. On nights with simultaneous PSG and actigraphy recordings, Spearman correlation coefficients were obtained for each sleep variable to determine the degree of correlation between PSG and actigraphy. The actigraphy measurements from all nights were used to assess night to night sleep variability.

Results:
In 11 males with ASD, correlations between PSG and actigraphy were statistically significant for Total Sleep Time, Sleep Efficiency, and Sleep Latency (r = 0.95, 0.95, and 0.99 respectively). The correlation for Wake Time after Sleep Onset was not statistically significant (r = 0.8). Results for night to night variability of the sleep/wake cycle are currently being analyzed.

Conclusions:
Actigraphy is technically comparable to PSG in measuring sleep latency, sleep efficiency, and total sleep time in children with ASD. Actigraphy is less sensitive in detecting wake time after sleep onset.

A systematic review was conducted of the literature published after 1950 on the diagnostic value of tests for differentiating between septic arthritis and transient synovitis in the acutely irritable pediatric hip, which defines septic arthritis as >50,000/mm3 leukocytes in the joint aspirate, positive gram stain of joint aspirate and bacterial growth on joint aspirate or blood culture.

Results:
A total of 743 abstracts were screened and 24 full articles were reviewed. Four studies were found to meet the inclusion criteria. The articles were for methodology, sources, sources of bias, ability to be generalized and diagnostic value. The conclusion thus far of this review is that there are clinical predictors which based on study design and results of the study have been shown to be effective in distinguishing between the two conditions. It is still not clear which of the predictors are of the most diagnostic value.

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Conclusion: Even though pre-operative RD is com-
mon in patients, performing comple-
tion angiography following hybrid and CABB-only procedures did not signif-
ically decrease their post-operative GFR. Our findings suggest that post-
hybrid or post-CABB-only completion coronary angiographies are safe from a renal function stand point.

A Meta-Review of Two Methods of Treating Radial Head Fractures
Christopher M. Kidd
Patient-Oriented Research

Background: Fractures of the radial head are a com-
mon injury of the upper extremity and are notoriously difficult to treat. Two methods used to treat these injuries are arthroplastic replacement of the radial head and a reparative open-
reduction procedure utilizing internal fixation devices. There is currently no consensus regarding which of these is the preferable method.

Objectives: To utilize a directed literature review in an attempt to determine which of the two surgical procedures described is associat-
ed with a better functional outcome.

Methods and Materials: Medical databases were searched for prospective and retrospective trials which documented outcomes following radial head arthroplasty or ORIF. Those that met inclusion requirements govern-
ing procedures, follow-up, and out-
come measurement were analyzed for outcome data. Data were grouped based on the severity of the initial injury and subsequently evaluated statistically.

Results: A total of 96 radial heads were replaced with prostheses and 93 were repaired using open reduction with inter-
nal fixation. Of the patients who under-
went arthroplasty, surgical outcomes were 40% good, 38% good, 15% fair, and 8% poor. Of those who underwent ORIF, outcomes were 46% excellent, 38% good, 11% fair and 5% poor.

Conclusions: Statistically, the two procedures described above have similar out-
comes, though further examination of the data may reveal that injuries of varying severity are better treated with different methods (these data have been calculated but did not fit here).

Acknowledgements: Dr. Donald Lee, Vanderbilt University Medical Center.

Expert Preception in Radiologists: an fMRI Study
Ronald Loch
Patient Oriented Research

Introduction: As radiology residents complete their training to become board-certified radiologists, they become able to meticulously discriminate and scruti-
nize subtleties in patients’ radiographs that help them diagnose normal or dis-
eased states. The radiologists’ ability to quickly and consistently identify these subtleties represents the pres-
ence of a highly specified expertise that is absent in the general population of non-radiologists.

Methods and Materials: Using functional magnetic resonance imaging, we studied four non-radiolo-
gists and four first-year radiology resi-
dents, comparing the brain activation patterns seen in these two groups when they viewed stimuli such as everyday objects, faces, or radi-
ographs. During the fMRI experi-
ments, the subjects participated in a one-back-identity task. The fMRI data for each subject was coregistered to a corresponding high resolution T1 weighted image volume, which was then transformed to Talairach space for a voxel-by-voxel based analysis.

Results: The voxel by voxel analysis showed that the radiologist had a significantly greater increase (p(Bonferroni)=0.001) in an area on the left cerebral cortex located within Brodmann’s area 37, than controls, in fMRI signal when viewing radiographic stimuli relative to viewing every day object. Additionally, there was a strong corre-
lation between the subjects’ accuracy during the one-back-identity task and the degree of activation in this area (R2=0.82). Other areas of significant activation include Brodmann’s area 6 (right) and Brodmann’s area 8 (right).

Conclusions: Already at this stage in their training, the 1st year radiologists do show increased activity in an area on the fusiform gyrus (contained within Brodmann’s area 37). In general, area 37 has been implicated in object recognition, so it is not surprising that there is a neural substrate within this area that is activated in 1st year radiologists. Other areas activated include Brodmann’s areas 6/8 and 19. One hypothesis that can be offered for this curious result is that the radiology res-
idents moved their eyes more during the radiographic stimuli and analysis of spatial locations of certain tissues in the radiograph, respectively.

Acknowledgements: Isabel Gauthier PhD and Calum Avison PhD.

Functional Outcome and Patient Satisfaction Following Open Treatment of Recalcitrant Lateral Epicondylitis
Mark Newton
Patient-Oriented Research

Background: Lateral Epicondylitis, or tennis elbow, is a fairly common, painful condition. It typically presents as intense, action limiting pain localized over the lateral epicondyle. There is not enough known about the surgical procedures to treat tennis elbow, and this study adds to the knowledge base and gives a basis for prospective trials at Vanderbilt University Medical Center (VUMC).

Objectives: To determine the functional results and overall patient satisfaction following a partial extensor origin debridement and partial ostectomy for recalcitrant lateral epicondylitis.

Methods and Materials: Eighty-seven (87) patients (48 males and 43 females) (91 elbows) were retrospectively reviewed following an open lateral epicondylar release. The mean (median) age was 45.1 (45.5) years. 61 surgical releases were per-
formed on the dominant arm. The average follow-up was 49 months (range 10 to 97). All patients were contacted via telephone. Outcome cri-
teria including Quick DASH (O = best score to 100 = worst score) and patient satisfaction (1 = very satisfied to 4 = very dissatisfied) scores were obtained on all patients. A Spearman’s rank correlation coefficient test was performed to determine whether age, sex, hand dominance, length of symp-
toms, worker’s compensation or number of steroid injections signifi-
cantly affected the Quick DASH and patient satisfaction scores (p < 0.05).

Results: Quick DASH Scores: The overall mean and median Quick DASH scores were 12.16 and 2.72, respec-
tively. The mean (median) scores for men and women were 11.83 (2.77) vs. 14.31 (4.54), respectively. The mean (median) scores for non-workman’s compensation and worker’s compen-
sation patients were 4.9 (1.1) vs. 16.5 (6.8), respectively. Patient Satisfaction Scores: The overall mean and median patient satisfaction score was 1.3 and 1. The mean (median) scores for men and women were 1.25(1) and 1.37(1), respectively. The median (mean) scores for non-workman’s compensation and worker’s compensation patients were 1.02(1) vs. 1.47(1), respectively. Negative prognostic factors affecting overall outcome were female patients, work-
man’s compensation, and non-domi-
nant arm (p < 0.001).

Conclusions: Partial extensor origin debridement and partial ostectomy for recalcitrant lateral epicondylitis is well tolerated. High functional DASH scores and patient sat-
isfaction scores are found. Negative prognostic factors include female patients, worker’s compensation and surgery on the non-dominant arm.

Using Capnography to Monitor Respiratory Function in Infants Receiving a Lumbar Puncture
Megan O’Neill
Patient Oriented Research

Background/Problem: Fever is among the most common pre-
senting complaints of infants in the Emergency department and may be the only presenting symptom of a serious bacterial illness. Therefore, it is con-
sidered standard of care to perform lumbar puncture on febrile neonates to rule out life threatening meningitis. There are currently two positions used to access the L3-L4 intervertebral space. Both involve flexion of the back and compression of the thoracic cavity. This restriction may lead to res-
piratory compromise in sick infants.

Objectives: We plan to compare standard indicators of respiratory function (oxygen satura-
tion, heart rate, and respiratory rate) to capnography (monitoring of end-tidal CO2 (ETCO2)). We will also evaluate the effect of positioning on the indica-
tors of respiratory function.

Materials and Methods: We plan to enroll 100 patients age 0-2 years who will receive an LP in the ED. Patients will be randomized to one of two positions (sitting vs. lateral decubitus). A Nellcor ETCO2 monitor will be used to assess ETCO2 5 min-
utes before, during and 5 minutes after the procedure. Oxygen saturation, heart rate, and respiratory rate will also be recorded by the Nellcor moni-
tor. The data will be stored and ana-
yzed using ProFox software.
Characterization of Cardiac Ankyrin Repeat Protein (CARP) Localization and Trafficking within Endothelial Cells

Jill Richman
Patient-Oriented Research

Background:
Angiogenesis, the formation of new blood vessels, is a key component of wound healing, a process which is often impaired in the diabetic state. Cardiac ankyrin repeat protein (CARP) is a transcriptional cofactor previously shown to have a role in promoting angiogenesis. CARP (Ankrd1) is a 319 amino acid intracellular protein found in the cytoplasm associated with the sarcomeric protein titin and in the nuclei of cardiomyocytes and skeletal muscle cells.

Objective:
The purpose of this study is to characterize the localization and regulation of movement of CARP within endothelial and vascular smooth muscle cells.

Methods and Materials:
To examine CARP trafficking, plasmid vectors containing a CARP-fluorescent tag fusion protein were constructed. The fluorescent proteins mVenus and moneo-DeRed were added to the C-terminus of CARP, and the recombiant fragment cloned into the pCDNA4/TO/mC-Myc-HisA plasmid.

Results:
These vectors are being used to transfect and express the fluorescently tagged CARP in endothelial, vascular smooth muscle and, as a control, skeletal muscle cells. The plasmid vectors have been tested in 293A cells, which showed translation and expression of the fusion proteins by wide-field and confocal fluorescent microscopy.

Conclusions:
Fusions of CARP and fluorescent proteins have been successfully constructed and are being used to investigate CARP’s intracellular trafficking. The effects of cellular stretch and cytokines on CARP will be examined as well. Determining the localization and movement of CARP in the cells of the vasculature may lead to a better understanding of its role in angiogenesis and how it may promote wound healing.

Acknowledgments:
Co-authors: Susan Samaras and Jeffrey Davidson.

A Technique for Carpal Tunnel Injection that Minimizes the Risk of Median Nerve Injury

Elizabeth Rinker
Patient-Oriented Research

Background:
Local steroid injection is one of many recommended treatments for carpal tunnel syndrome. Improper needle placement may result in injection injury to the median nerve at the wrist, leading to exacerbation of symptoms, permanent neurological deficit, or both. There is currently no consistency in the literature as to which of the many injection techniques described is most beneficial to the patient in terms of avoiding injury to the median nerve.

Objective:
To establish a safe technique for the injection of steroids into the wrist to treat carpal tunnel syndrome that minimizes the risk of associated damage to the median nerve.

Methods and Materials:
Part 1: 36 cadaveric wrists were dissected to determine the relationships of the radial artery (RA), flexor carpi radialis (FCR) tendon, palmaris longus (PL) tendon, median nerve (MN), flexor carpi ulnaris (FCU) tendon, and ulnar bundle (UB) at the level of the wrist flexion crease. The wrist width was recorded with a caliper. The distance of each structure relative to the radial aspect of the wrist was measured and these measurements were converted into percentages of total wrist width. Part 2: Two 18 gauge hypodermic needles were inserted into 32 additional cadaveric wrists. Needles were inserted into 2 potential sets of sites of injection: 1.33% and 66% of the total wrist width ranged from 5 mm to 15 mm (8% to 28% of total wrist width). 18 mm to 35 mm (31% to 59%), and 35 mm to 56 mm (63% to 86%), respectively. Using the 33% and 66% injection sites there were no penetrations of the MN and 6 penetrations of the UB. Using the 30% and 60% injection sites there were 2 penetrations of the MN and no penetrations of the UB. There were no penetrations of the radial artery using either set of injection sites.

Conclusions:
There is anatomic variation concerning the location of the RA, MN, and UB. The 30% and 60% injection sites appear to be relatively safer than the 33% and 66% injection sites, but the 30% injection site appears to be the safest. The FCR tendon should be used as a guide for injections on the radial side of the wrist.

Acknowledgements:
Donald H. Lee, MD, Department of Orthopaedic Surgery, and Rafe Donahue, PhD, Department of Biostatistics, Vanderbilt University Medical Center.

The Selective Amygdalohippocampectomy: Assessing Surgical Outcomes at Vanderbilt University

Stephen Stahr
Patient-Oriented Research

Background:
Epilepsy is a disease which is characterized by recurrent unprovoked epileptic seizures and it affects as many as 50 million people worldwide. One form of epilepsy referred to as partial epilepsy is due to pathology which can be localized to a particular area of the brain; the temporal lobe is the most common pathology in cases of partial epilepsy. When temporal lobe epilepsy is due to hippocampal sclerosis, the current treatment is frequently the selective amygdalohippocampectomy. The outcome of this procedure has never been studied at Vanderbilt.

Objectives:
To assess the outcome of the selective amygdalohippocampectomy at Vanderbilt and to evaluate the prognostic significance of certain available variables.

Methods and Materials:
This study was completed by reviewing patient charts and performing a large number of telephone surveys of patients who had undergone a selective amygdalohippocampectomy at Vanderbilt.

Results:
Although the data analysis has not yet been finalized, some interesting observations have been made on initial overview. For example, out of 30 patients who had no contradictory preoperative tests, 70 percent were classified as Engel classification IA, they were essentially cured of their seizures. This seems consistent with other published results. Completion of analysis will likely yield more interesting results.

Conclusions:
The selective amygdalohippocampectomy at Vanderbilt is an effective method for treating hippocampal sclerosis. This study has already demonstrated the efficacy of the procedure; it also has demonstrated that a different method of storing patient data from the one currently in use may facilitate future analysis of patient outcomes.

Acknowledgements:
John Spoonsor, MD, and David Sun, MD, PhD, Department of Neurological Surgery, Vanderbilt University Medical Center.
Evaluating the Identification of Patients with Renal Malignancies and Positive Smoking History

John Stringham
Patient-Oriented Research

Background/Problem: Renal cell carcinoma (RCC), while relatively rare, is still a significant etiology for malignancy in the United States, with 39,000 diagnoses in 2006, resulting in 13,000 deaths. The incidence of this disease has been increasing with time. Smoking has been found to be a major modifiable risk factor for RCC, increasing risk of development of the disease by two-fold. Smoking has also been found to increase mortality from RCC as well. It is well-known that smoking in the United States is a large problem, with 16% of all cancers being attributable to smoking. Tobacco use has also been found to increase the likelihood of adverse events post-operatively. It is unknown how effective current initiatives are in identifying RCC patients who are current smokers, and how often effective treatment is begun.

Objectives: To assess the effectiveness of initial identification of individuals with a past or current smoking history, examine the use of tobacco in this population, and evaluate the effectiveness of follow-up in those patients with a current smoking habit at diagnosis.

Methods and Materials: A systematic retrospective electronic chart review of all individuals undergoing nephrectomy for any reason between 1/28/2004 and 2/23/2006 was performed. Documents examined included the initial urologic consultation, the preoperative evaluation, last follow-up clinic visit note, and all problem lists from time of diagnosis to last follow up. A comprehensive smoking history was gathered, as well as how often smoking history was recorded in the electronic record.

Results: Records from a population of 379 consecutive patients were examined. Seventy percent of nephrectomies were from RCC. 8.75% were transitional cell carcinoma of the renal pelvis, and 11.25% were from benign disease. From these records, at the first presentation of all patients, 259 (66.06%) did not have their smoking history described on their initial problem list, while 128 individuals (37.27%) did not have smoking history recorded on their initial clinic visit. For current smokers, 69% were identified as such on initial clinic visit. Using preoperative evaluation data, current smokers had a 0.91 pack per day (ppd) habit (95% CI 0.86-0.96), and had 25.64 mean pack-years of use (95% CI 23.87-27.43); mean length of follow-up of current smokers was 268.2 days (95% CI: 243.6-292.7). When the follow-up data was examined, only 7.5% of current smokers showed a positive change in their smoking habits, while 42.5% showed no change. 51.25% of current smokers had no data recorded on their habit during the follow-up period.

Conclusions: Smoking is considered to be the strongest risk factor associated with cancers of the kidney and has been shown to be associated with increased mortality and increased complications in the perioperative time period. Sixty-nine percent of current smokers were correctly identified on initial presentation. However, the electronic problem list of the record system at a major university hospital was underutilized, with only 25% of current smokers listed as such using this document. Previous studies have shown that a problem list can increase health care provider intervention by three-fold. If used effectively, the problem list can be beneficial in helping patients undergo smoking cessation.

References:

Acknowledgements:
Sam Chang, MD, Lilian Nanney, PhD, Sanjay Patel, Chris Welty and Lee Cannan, Vanderbilt University Medical Center.

Brain Manganese Deposition in High Risk Neonates
Josie Vitalize
Patient-Oriented Research

Background/Problem: Manganese (Mn), an essential metal needed for normal growth and development, can be neurotoxic upon excessive environmental or dietary exposure. Sick infants requiring parenteral nutrition (PN) may be at increased risk of Mn toxicity because current neonatal PN solutions contain high Mn concentrations and PN bypasses intestinal control of Mn absorption. In addition, sick infants have impaired Mn excretion and reduced iron stores; iron deficiency increases uptake of Mn into the brain. Mn is a paramagnetic element and can be detected by Magnetic Resonance Imaging. The impact of extended exposure to parenterally delivered dietary Mn on the neonatal brain has not been scientifically addressed.

Objectives: To identify neonatal populations at increased risk of excessive brain Mn deposition and altered cognitive and motor development based on their dietary parental Mn exposure.

Methods and Materials: Longitudinal assessments of cognitive (executive functioning battery), neurodevelopmental (Bayley III Scales of Infant Development), and psychophysiological (event-related potential) measures will be correlated with blood Mn levels and brain Mn deposition. There will be an experimental group of 40 infants receiving PN in the VCH NICU, plus three control groups: a MRI control group (n=20); a gestational age-matched control group (n=40); and a corrected age-matched control group (n=40).

Results: To date, 7 infants have been enrolled in the experimental group and 13 infants have been enrolled as MRI controls.

Conclusions: It is hypothesized that compared with unexposed age-matched controls, infants receiving prolonged Mn-supplemented PN will have increased deposition of Mn in their brains and lower scores on neurodevelopmental, cognitive, and psychophysiological assessments.

Acknowledgements
Judy Aschmer, MD, Professor of Pediatrics, Chief of Neonatology, Vanderbilt Children’s Hospital.

A Brief Clinical Intervention Opens The Door for Discussions about Violence Risk Factors

Courtney Walkowski
Patient-Oriented Research

Background: Childhood aggression, a common child behavior problem, and poor parental discipline are two risk factors for violence later in life.

Objective: To determine whether a brief clinic-based intervention affects parents’ willingness to discuss child behavior and discipline strategies with their pediatrician.

Methods and Materials: Thirty-five consecutive parents with children less than 7 years of age presenting for a well child visit were included in the program. The next (i.e., required) component of the visit. Fifty-four additional parents were recruited from a “convenience sample”, based on their willingness to participate. The intervention, viewed in the waiting room, was the Play Nicely CD which provides the basics in managing childhood aggression. Parents who viewed at least four aggression management strategies (< 5 minutes) were recruited for an anonymous personal interview; no parent declined.

Results: The average age of the 35 participants (95%) was 27 years, 50% had at least some college education and 48% were African-American. After the intervention, 100% were pleased that their pediatrician provided the Play Nicely Program for parents with young children. 74% parents were more willing to discuss child behavior with their pediatrician. 77% were more willing to discuss discipline options. No parent reported being less willing to discuss these topics. Parents were asked what they heard or saw in the program to make them more willing to have discussions. Parents responded with comments such as: “The program forced me to think about issues that I previously had never considered” and “The videos made me think of specific problems I’ve been having and reminded me to ask about them.”

Conclusions: This is the first study to find that a brief clinic-based intervention increases parents’ willingness to discuss child behavior and discipline strategies with their pediatrician.

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their pediatrician. Increasing communication between parents and professionals regarding these anticipatory guidance topics has implications for violence prevention. Future studies should measure whether more discussions actually occur.

Acknowledgements:
S. J. Scholer, MD, MPH, Vanderbilt University Medical Center and L. Bickman, PhD, Vanderbilt University.

Frequency of Community-Associated Methicillin-Resistant Staphylococcus Aureus (CA-MRSA) Nasal Colonization in Adolescents

Michelle M. Walther
Patient-Oriented Research

Background:
Prior studies suggest that nasal colonization with CA-MRSA has increased in the healthy pediatric population. However, many of these studies are weighted heavily towards infants and young children, despite the growing problem of severe CA-MRSA sepsis in adolescents. Therefore, we sought to describe the frequency of CA-MRSA nasal colonization in healthy adolescents.

Methods and Materials:
Adolescents ages 11-18 were recruited from a community pediatric practice in the summer of 2006. Nasal swabs were collected and enriched in tryptic soy broth overnight. An aliquot from each sample was cultured onto paired mannitol salt agar plates with/without 4 µg/mL of oxacillin and incubated at 37°C for 48 hours. After subculturing to blood agar plates, all putative staphylococcal isolates underwent coagulase testing. To confirm methicillin resistance, amplification of the mecA gene by PCR was performed.

Results:
One hundred thirty-three subjects were enrolled. Forty-eight subjects were nasal carriers of MRSA (36.1%), 15 of which were methicillin-resistant (31%, 11.2% overall). There were no differences in overall staphylococcal colonization or MRSA colonization based on demographic characteristics. There has been no significant change in the frequency of MRSA colonization in adolescents in our community since 2004 (900 subjects 9.1% vs. 48/133 subjects 11.2%, p=0.52).

Conclusion:
In this study, 11.2% of adolescents were nasal carriers of MRSA. This suggests that MRSA nasal colonization is an ecologically persistent phenomenon in our community. Knowing that adolescents may represent an “at-risk” population for severe staphylococcal sepsis, further understanding of the relationship between carriage and infection is crucial in defining the pathogenesis of staphylococcal disease.

Acknowledgements:
C. Buddy Creech (mentor), Kathryn Edwards, Nathan R. Starke and Belinda G. Johnson.

Iontophoretic Administration of Corticosteroids in the Treatment of Lateral Epicondylitis

Kenneth Durham Weeks, III
Patient-Oriented Research

Background/Problem:
Lateral epicondylitis (LE) is the most prevalent disorder of the elbow in adults. Pain associated with this debilitating musculoskeletal condition affects roughly 1% of patients attending general medical practices, and upwards of 15% of patients working in highly repetitive hand task industries. Several pain-relieving interventions are available for treating LE; however, there is insufficient evidence for a specific standard of care. Iontophoresis uses a small, external electric current to drive topically applied water soluble drugs through the outer layers of the skin. Although previous studies have found iontophoretic administration of corticosteroids to improve function, range of motion, and decrease pain in patients suffering from LE in the short term, there is inconclusive evidence regarding its long term effectiveness.

Objective:
This double-blinded study aims to investigate the short and long-term therapeutic efficacy of iontophoresis in patients suffering from an episode of LE.

Methods and Materials:
Enrolled subjects receive a physical exam of the affected elbow and pain is assessed using the Disabilities of the Arm Shoulder and Hand (DASH) survey as well as the Visual Analog Score (VAS). Patients are then randomized into active and placebo groups. On six different occasions within two weeks, patients in the active arm receive iontophoretic administration of dexamethasone, while the placebo arm receive saline solution applied to the affected elbow. Follow-up clinical assessments of the affected elbow are conducted one week and one month post treatment and include a physical exam, DASH, and VAS scores.

Results:
Enrollment and results of this clinical trial are pending.

Conclusions:
Analysis and conclusions are pending.

References:

Acknowledgements:
Donald H. Lee, MD and Julie M. Daniels, Vanderbilt Orthopaedic Institute.
Education

Emphasis experiences in the 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 education is developed and evaluated in medical school and residency settings.

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 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?

Don Moore is Director, Division of Continuing Medical Education at Vanderbilt University School of Medicine. 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, computerized order entry, electronic medical records, and evidence-based medicine. 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.

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Vanderbilt Emphasis Forum Education

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

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