Cardiac Function in Long-Term Survivors of Hodgkin's and Non-Hodgkin's Lymphoma After Radiation Therapy/Anthracycline Chemotherapy

Introduction: Radiation therapy and anthracycline chemotherapy are integral components of the treatment of Hodgkin's Lymphoma (HL) and Non-Hodgkin’s Lymphoma (NHL). However, these therapies, both independently and in combination, have been associated with cardiovascular disease sequelae through generation of free radicals that disrupt DNA strands.

Objectives: The goals of this study are to determine the frequency of alterations in cardiac functions and relative myocardial perfusion in long-term HL and NHL survivors treated with mediastinal radiation therapy (mRT) and/or anthracycline chemotherapy.

Methods: We have conducted a retrospective analysis of HL and NHL patients treated at the University of Rochester Wilmot Cancer Center from August 1991 to June 2007 who had either single photon emission computed tomography (SPECT) or multiple gated acquisition (MUGA) scans. These scans were ordered to follow cardiac function post mRT and/or anthracycline-based chemotherapy as part of routine screening regardless of symptomology. Patients were split into 3 groups: mRT only, chemotherapy only, and mRT and chemotherapy. MUGA scans evaluate left ventricular ejection fraction (LVEF), while SPECT scans evaluate LVEF, myocardial ischemia, and end diastolic and end systolic volume indices (EDVI and ESVI, respectively). Clinically relevant cut-offs were used to estimate normal ranges.

Results: There were a total of 118 patients with 87 HL and 31 NHL. 34 patients received mRT only, 17 chemotherapy only, and 67 both mRT and chemotherapy. Abnormal LVEF was noted in 5.9% of mRT only patients, 17.6% of chemotherapy only patients, and 23.8% of mRT and chemotherapy patients. Myocardial ischemia was noted in 3.7% of mRT only patients, 18.2% of chemotherapy only patients, and 14% of mRT and chemotherapy patients. Abnormal EDVI was noted in 27.2% of mRT only patients, 33.3% of chemotherapy only patients, and 26.3% of mRT and chemotherapy patients. Abnormal ESVI was noted in 4.5% of mRT only patients, 22.2% of chemotherapy only patients, and 34.2% of mRT and chemotherapy patients.

Conclusions: Based on these preliminary results, anthracycline-based chemotherapy appears to have more deleterious effects on clinical cardiac endpoints of HL and NHL patients than mediastinal radiation therapy. We are beginning to evaluate correlations between mRT/chemotherapy doses and cardiac endpoints, while analyzing pathogenesis of cardiac injury.
Are Filaggrin Mutations Responsible for Increased Transepidermal Water Loss?

Introduction: TransEpidennal Water Loss (TEWL) is a universally accepted objective measurement of barrier function in the cutaneous epithelium. Most atopic dermatitis (AD) subjects have increased TEWL measurements which is thought to be due to the breakdown of their skin barrier. Several null mutations in filaggrin, a protein in the skin's stratum corneum, have recently been linked to AD and ichthyosis vulgaris (IV). Studies have found filaggrin allele frequency in AD cohorts range from 8.8 to 33%. Therefore, it is likely that there are other mechanisms besides FLG mutations that explain the barrier defect observed in AD subjects. Objectives: This study will evaluate the FLG genotype with phenotype (TEWL) in three populations (nonatopics, AD and IV). It is our hypothesis that other barrier defects (genetic or acquired) may also explain the phenotype of enhanced TEWL in the AD group. Identification of such defects is the focus of my P.I.'s (Dr. Beck's) lab. In expression profiling studies they have shown dysregulation of several barrier proteins important for the integrity of tight junctions, adherens junctions and gap junctions suggesting that barrier defects extend beyond the cornified layer.

Methods: Our study enrolled subjects with AD (n=1), IV (n=1) and non-atopic healthy controls (n=9). Each subject signed an informed consent waiver, answered a questionnaire, and received a dermatological exam (including EASI measurements). We performed a series of 4 TEWL measurements on a non-sun exposed area of the volar forearm over the course of two visits. Each subject also had a non-lesional (and optional lesional) skin biopsy near the site of the TEWL measurement. DNA was isolated for later analysis.

Results: This project allowed me to draft and develop the forms and questionnaires, obtain human subject research certification, and enroll subjects (11 to date) in the study. I learned how to obtain TEWL measurements, take EASI measurements and isolate human DNA from blood samples. Subjects continue to be enrolled to achieve a statistically meaningful number for genotype/phenotype comparisons.

Conclusion: These results support and extend the evidence that there is dysregulation of proteins important for epidermal maturation/differentiation and barrier function in AD with some distinct signatures. The fact that these abnormalities are observed in non-lesional skin suggests that they are not simply a consequence of disease-specific inflammation.

References:
Basic Science and Clinical Research

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Prehospital Spinal Immobilization is Not Beneficial and May Complicate Care Following Gunshot Injury to the Torso.

Background:
Gunshot wounds (GSW) are a significant public health problem, accounting for 19% of all trauma deaths in the United States. Prehospital spinal immobilization (PHSI), which includes the use of a rigid cervical collar and full back-board, is routinely applied to patients with isolated GSW; however the appropriateness of this is unclear. The theoretical benefit of PHSI is prevention of secondary spinal cord injury (SCI) as a consequence of excessive movement in patients with unstable fracture of the vertebral column. This must be weighed against the potential problems of delaying time to definitive surgical care and increasing difficulty of airway management.

This study sought to evaluate the benefits and disadvantages of PHSI for isolated GSW patients in order to examine whether routine use of the procedure in this population should continue. The objectives were to document the incidence of patients potentially benefiting from PHSI as well as acuity, need for airway placement, neurological progress, and prehospital time frame as potential draw-backs of PHSI in these patients. The hypothesis was that the disadvantages of routine PHSI for torso GSW would outweigh the potential benefit.

Methods:
Retrospective analysis of the National Trauma Databank (NTDB) over 60 months of all GSW patients was conducted. Patients with spine injuries and surgical stabilization were identified using ICD-9 codes. Additionally, analysis of torso GSW patients from Strong Memorial Hospital (SMH), an urban level I trauma center, over 41 months was conducted. Medical records of patients with spine injuries were further reviewed to collect data regarding spinal injury characteristics and neurological status.

It was hypothesized that patients with SCI following GSW had permanent neurological deficits, thus PHSI was considered potentially beneficial in patients with unstable spine fractures without SCI requiring operative stabilization. The need for emergent surgical intervention was defined as an emergency department (ED) disposition to the operating room (OR) or death in the ED.

Results:
There were 75,210 subjects with GSW identified in the NTDB. The rate of any spinal injury was 4.3% following GSW. Only 26 (0.03%) NTDB subjects potentially benefited from PHSI. Emergent surgical intervention was required by 43% of NTDB subjects and intubation in the emergency department was required by 17.5% of NTDB subjects.

There were 357 subjects with a torso GSW identified in the SMH database. There was a 9.2% rate of any spine injury following a torso GSW. No subject from SMH potentially benefited from PHSI. No subject from SMH with SCI had any neurological improvement or worsening by discharge and no
subject developed a deficit during admission. Emergent surgical intervention was required by 54.5% of SMH subjects and intubation in the emergency department was required by 40.6% of SMH subjects. Prehospital scene time of SMH subjects was longer than transport time (12.6 min. vs. 9.3 min., p<0.01), with an average ratio of time on scene to time in transit for each patient of 1.7.

Conclusions:
The number of patients that potentially benefit from PHSI appears extremely low. Conversely, a prominent need for emergent surgical intervention and intubation exists in these patients. Most GSW injuries occur in an urban setting in proximity to a level I trauma center. When considering the delay to definitive surgical care, potential to complicate airway management, and lack of neurological progress against the small potential benefit, routine PHSI for isolated torso GSW appears unjustified.
A Pilot Investigation of Colorectal Cancer Screening for Awareness, Practices, and Recommendations on the Navajo Reservation

Abstract: While increasing colorectal cancer screening is considered a cornerstone for decreasing colorectal cancer mortality, much is unknown about how to increase colorectal cancer screening rates among the Navajo people. Colorectal cancer first develops with few, if any, symptoms. If symptoms are present, the most common symptoms include abdominal pain, rectal bleeding, altered bowel habits, and involuntary weight loss [1]. Less common symptoms include nausea and vomiting, malaise, anorexia, and abdominal distention [2]. Colorectal cancer occurs in men and women, the majority of cases being diagnosed in people aged 50 years or older. The risk of developing colorectal cancer increases with age and a family history of colorectal cancer or colorectal polyps may increase a person's risk of developing colorectal cancer.

The Navajo Nation population has a 23% median age of 45 years and older compared to 34% for the general US population. Between 1990 and 2000 Censuses, there was a 41% increase in the number of Navajo persons 64 years and older, compared to a 16% increase for the general US population. Thus, the number of Navajo people reaching the age bracket requiring colorectal cancer screening will increase substantially in the coming years.

A literature review suggests that no empirical research has been conducted on or near Indian Reservations that was focused primarily on colorectal cancer screening awareness, knowledge, or recommendations for American Indian populations. However, a single Navajo family with hereditary nonpolyposis colon cancer (HNPCC) was investigated in 1985 [3] with a follow-up on the same family in 1991 [4]. Later in 1991 and 1996, the same Navajo family was further evaluated with genetic counseling and a genetic investigation revealed a mutation that could help explain this family's history of colon cancer. According to one of the authors of the study, who is a physician on the Navajo Reservation, observations of this family began in 1983 and has, since then, resulted in education and recommendations for cancer surveillance and management for the families with which they have been in contact. Unfortunately, no data has been collected on what the colorectal cancer screening awareness is among the Navajo people to improve approaches to education and recommendations for Navajo people living on the Navajo Reservation.

Objectives: This pilot study has three phases which test a draft questionnaire and establish a preliminary baseline for colorectal cancer screening awareness and knowledge among Navajo people living on the Navajo Reservation. Another aim of this investigation is to draw on Navajo Area Indian Health Service (NAIHS) provider practices and recommendations to assess what strategies have worked and what has not worked in their experience working with Navajo patients.

Methods: Anonymous assessments were voluntarily self-administered at two Navajo tribal fairs: the Northern Navajo Nation Fair and the Western Navajo Nation Fair among Navajo male and female participants aged 18 and over.

Phase 1 of this pilot study consisted of 56 Navajo male and female participants aged 40 and
over who were recruited from four communities on the Navajo Reservation. The participants were divided into seven focus groups of 6 to 8 people. The focus groups were conducted in both the Navajo and English languages. Qualitative analysis will be used to analyze focus group discussions to determine the themes and patterns related to cancer and colorectal cancer screening knowledge.

Phase 2 of this pilot study consisted of 20 Navajo male and female outpatients aged 40 and over who were recruited from two hospital populations on the Navajo Reservation. The participants were individually interviewed using the draft questionnaire entitled, "A Pilot Study to Test a Questionnaire and Gather Preliminary Data on Navajo Knowledge and Awareness of Colon Cancer Screening" in either the Navajo or English languages. Recordings of their Likert Scale responses will be imported to STATA for statistical analysis to characterize participants’ colorectal cancer screening knowledge. The qualitative comments for both phases 1 and 2 will be analyzed using Teufel-Shone, Siyuja, T., Watahomigie, H.J., & Irwins, S. [7] independent-consensus method of analysis that takes into account the individual perspectives of native and nonnative researchers and a consensus is reached during an analysis team meeting.

Phase 3 of this pilot study involves a review of NAIHS existing data on provider practices and recommendations gathered from the NAIHS Division of Epidemiology and Disease Prevention. A total of 37 NAIHS providers representing five NAIHS facilities completed the web-survey.

Results: All data for each phase has been collected and is still undergoing analysis as outlined in the methods. The results will be reported to the Navajo Nation Human Research and Review Board, project advisory committee, University of Arizona College of Medicine mentoring faculty team, Western Navajo Agency Council, Northern Navajo Agency Council, Navajo Medicine Man Association, and R25 Postdoctoral Arizona Cancer Center's Cancer Prevention and Control Grand Rounds.

References
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The Association of Complement Factor B (CFB), High-Temperature Requirement Protein Al (HTRA1), and LOC387715 with Age-Related Macular Degeneration

ABSTRACT

Purpose: To determine if the LOC387715 (G>T; Ala69Ser), HTRA1 (G>A), and CFB (T>A; Leu9His) single nucleotide polymorphisms (SNPs) are associated with wet and dry AMD in a diverse Southern Californian population.

Methods: Total DNA was isolated from 103 AMD subjects and 126 age-matched control subjects. The LOC387715, HTRA1, and CFB genes were amplified by polymerase chain reaction and digested with PvuII, SfiI, and BstI, respectively, in order to determine the presence or absence of certain SNPs in these genes. The SISA statistical analyses program was used to quantitatively describe associations between the variable alleles and the AMD and/or control groups.

Results: In examining the G>T (Ala69Ser) SNP in LOC387715 exon 1, the GG genotype was found to be protective against wet AMD (OR=.3448; 95% CI [.1888-.6299]; p=.000220). Additionally, the GT genotype was associated with wet AMD (OR=1.8908; 95% CI [1.0723-3.3339]; p=.010038), while the TT genotype was associated with both wet and dry AMD (wet: OR=2.5224; 95% CI [1.0241-6.2128]; p=.023209); (dry: OR=3.6111; CI[1.087-11.9964], p=.034119). In examining the G>A SNP in the promoter region of HTRA1, the GG wild type variant was found to be protective against wet AMD (OR=.4504; 95% CI [.2597-.7813]; p=.001839), while possession of one A allele was found to be associated with wet AMD (OR=2; 95% CI [1.13-3.5397]; p=.006648). In examining the T>A (Leu9His) SNP in CFB exon1, no significant association with the AMD or the control group was found for either the TT or the TA genotype. None of the individuals studied were found to possess the AA genotype.

Conclusions: In regards to LOC387715 and the G>T SNP, the GG genotype appears to be protective against wet AMD. Possession of one T allele is a risk factor for wet AMD, while possession of two T alleles is a risk factor for both wet and dry AMD.

In regards to the G>A SNP in the promoter region of HTRA1, the GG genotype appears to be protective against wet AMD, while possession of one A allele is a risk factor for wet but not dry AMD.

For the T>A SNP in CFB exon 1, neither the TT nor the TA genotype appears to be significantly associated with the AMD or the control population. No individuals possessing the AA genotype were documented in this study.

References


Age-related Changes in Human Memory:  
The Role of Prefrontal Cortex in Maintaining Successful Memory Performance

Abstract:
While complaints of memory impairment are common among older adults, our understanding of age-related changes in the structure and function of the human brain remains limited. Even in the absence of overt pathology, aging is associated with well-documented impairment of a variety of cognitive abilities, and neuroimaging studies consistently reveal age-related alterations in the patterns of neural activation elicited by memory tasks. Specifically, numerous studies report that while older individuals show decreased neural activity in some regions activated by younger adults, these individuals may also show increased activation in regions not utilized by the younger subjects.

Two major mechanisms have been proposed to account for these age-related increases in neural activity: dedifferentiation and functional compensation. While these mechanisms are not mutually exclusive, understanding the relative contribution of each to the generation of neural activity is central to understanding the activity's functional significance. If the activation of a particular region is due mostly to cortical dedifferentiation, then that activation may represent the spreading of neural "noise" outside of relevant circuits and into regions ill-suited to perform the necessary computations. Such activation would therefore be of little use to the individual. Alternatively, if an age-related increase in activation reflects the recruitment of new neural tissue in order to compensate for functional deficits elsewhere in the brain, then such activations could improve the individual's performance on the task at hand.

In the present study, we employ a recently developed multivariate approach to assess the role of lateral prefrontal cortex (PFC) in performing each stage of a delayed match-to-sample task. Initial results suggest that while older adults exhibit decreased use of hippocampal networks during the maintenance phase of the task, they simultaneously demonstrate increased interaction between lateral inferior frontal gyrus and posterior representations of the visual information being maintained. While still preliminary, these data support the view that age-related increases in PFC activity may represent functional compensation for deficits in medial temporal regions. By improving our knowledge of age-related changes in neural function, we hope to move one step closer to the ultimate goal of developing therapeutic countermeasures to the memory impairment observed in normal aging, neurodegenerative diseases, trauma, and stroke.
Histone Deacetylase Inhibitors Restore Runx2 Expression and Sensitize Osteosarcoma Cells to Chemotherapy

Abstract: Transcriptional repression of tumor suppressor genes by altered histone deacetylase activity has been implicated in cellular transformation. Furthermore, studies have shown that histone deacetylase inhibitors (HDACi) reverse this epigenetic process, inducing differentiation and cell cycle arrest as well as sensitizing cancer cells to chemotherapy and radiation.

Objective: We tested the hypothesis that HDACi treatment of osteosarcoma cells in vitro could revert the malignant phenotype by restoring the expression of genes involved in osteoblast differentiation and apoptosis regulation, notably the transcription factor, Runx2.

Methods: We treated human immortalized fetal osteoblasts (hFOB) and two osteosarcoma cell lines, 143B and TE85, with valproate, an FDA-approved anticonvulsant, or SAHA (vorinistat), a recently FDA-approved cancer therapy for cutaneous T-cell lymphoma. We determined the effects of HDACi on the transformed phenotype, including cell cycle progression, colony formation in soft agar, and sensitivity to chemotherapy. We also determined HDACi effects on the expression of genes involved in osteoblast differentiation, particularly Runx2, at both the RNA and protein levels.

Results: HDACi suppress the ability of 143B cells to form colonies in soft agar, an in vitro assay of tumorigenicity. In addition, HDACi treatment of TE85 and 143B cells induced a G2/M cell cycle arrest as detected by flow cytometric analysis of BrdU-labeled cells. 143B cells were also sensitized to doxorubicin by both HDACi's as detected by flow cytometric analysis of caspase3 cleavage. These biological effects correlated with restored Runx2 protein but not mRNA expression in TE85 and 143B cells.

Conclusions: The increase in sensitivity of 143B cells to chemotherapy provides promise for HDACi's as a useful adjuvant in treatment of osteosarcoma. HDACi treatment led to a partial reversion of the malignant phenotype of these two osteosarcoma cell lines, while concurrently increasing expression of Runx2, a key regulator of differentiation and apoptosis. Future studies will be aimed at linking the increased expression of Runx2 to the phenotypic changes in these cells as well as identifying downstream targets of Runx2 involved in these processes.

References:
Assessing the Concerns of SCI Patients in order to Improve Treatment

Objectives: To study the patient's changing perspective of personal well-being, activity level, and need for injury education as time increases following a spinal cord injury. To use this information to implement more patient-centered care.

Methods: Forty three SCI patients receiving care at University of Rochester Medical Center answered 77 questions measuring well-being, activity level, and need for injury education. Patients were placed into groups based upon time since injury.

Results: A total of 60.5% (n=26) of the patients in the study were injured within the last year, 14% (n=6) of the patients in the study had been injured for 1-3 years, and 14% (n=6) of the patients in the study had been injured for more than 3 years. Depending on the time since injury, the three groups showed different perceptions of well-being and activity level with the Wilks' Lambda significant at the $p=.00$ level. Patients injured 1-3 years ago perceived themselves as having the highest wellbeing and activity levels. Patients injured less than one year ago perceived themselves having the lowest wellbeing. Patients injured more than 3 years ago showed feelings of the lowest activity level. Based on our knowledge of a patient's time since injury, knowing their responses from the questionnaire, we can predict their perception of personal wellbeing and activity level 100% of the time. In addition, depending on time since injury, the three groups showed different SCI educational needs with the Wilks' Lambda significant at the $p=.00$ level. Patients injured 1-3 years ago reported the most need for further education on SCI issues. Patients injured for more than 3 years reported the least need. Based on our knowledge of a patient's time since injury, knowing their responses from the questionnaire, we can predict their educational needs 100% of the time.

Conclusions: This study showed that based on time since injury, patient feelings of wellbeing, activity level, and need for injury education can be predicted. These predictions can aid physicians in modifying treatment plans based on how long a patient has sustained an SCI.

References:
Functional Assessment of Neurogenic Intermittent Claudication in Patients with Lumbar Spinal Stenosis Using an Ambulatory Treadmill Test

Introduction: Spinal stenosis is a common cause of low back pain and the leading indication for lumbar surgery in the United States for persons over 65 years of age. The wide variation in rates of surgery reflects uncertainty about which patients are most likely to experience a reduction in pain or improvement in their walking tolerance. The introduction of new technologies to decompress stenotic spinal segments highlights the need to develop functional measures that optimize treatment matching.

Objectives: Develop a standardized treadmill protocol to measure symptom severity and the functional consequences of neurogenic intermittent claudication in patients with lumbar spinal stenosis. We hope to show that the ease of administering, and the reliability of results from the ambulatory treadmill test substantiate its use in the clinical assessment of patients with symptomatic lumbar spinal stenosis, and aids in the treatment decision making process.

Methods: AP is an 87 y/o Caucasian man with radiographically verified spinal stenosis and clinically diagnosed neurogenic claudication. Based on imaging studies, location of symptoms and clinical exam findings, AP was scheduled to receive an epidural steroid injection at the level of L2-L3. One day prior to injection, a treadmill test was conducted to assess baseline symptom severity and walking tolerance. The protocol requires the patient to walk at a constant speed of 1.2 mph at zero degrees inclination for as long as tolerable or for a maximum of 15 minutes. Symptom severity was assessed on the numeric rating scale (NRS) from 0 to 10. The primary endpoint measured was time to first symptoms (Tfirst). Secondary endpoints were total time walked, total distance walked, self-reported symptom severity at baseline (TO), 3 minutes (T3), 6 minutes (T6), 9 minutes (T9), 12 minutes (T12), and 15 minutes (T15), time to return to baseline (Trecovery), and area under the curve for pain plotted against time. Treadmill testing was repeated for a second time ten days following injection, and a third time 6 weeks post injection.

Results: AP's Tfirst decreased from 2 minutes, to 1 minute 18 seconds, and then increased up to 1 minute 50 seconds on the three successive trials. Total time walked, and total distance walked remained the same for each trial and were 15 minutes and 475 meters, respectively. The areas under the curve for symptom severity versus time for each of the three trials were 74.25, 40.5, and 57. Trecovery for the three trials was 1 minute, 2 minutes 42 seconds, and 30 seconds, respectively.

Discussion: Tfirst showed some variation between the three trials; however, it was felt that in this patient, Tfirst measures were not accurate on account of variation in prompting by the test administers necessary for patient feedback. Similarly the variation in Trecovery was felt to be due to prompting by the researchers, and precludes those data from further evaluation. The overall symptom severity as
measured by patient-reported NRS values and area under the curve decreased substantially during the assessment following epidural steroid injection at L2-L3. The patient's satisfaction with steroid injection for the treatment of his neurogenic claudication symptoms was measurably corroborated by the ambulatory treadmill test. Treadmill testing for the third time, 6 weeks post-treatment, reflected the wearing-off of the steroidal effects. **Conclusions:** Ambulatory treadmill testing is easy and safe to perform. With the proper patient instruction, we believe the test can be reliably and accurately used to functionally assess patients with neurogenic intermittent claudication pre and post-treatment.

**References**

Risk Factors for Chronic Lung Disease in a Population of Extremely Low Birth Weight Infants

General: Chronic lung disease (CLD, also known as bronchopulmonary dysplasia, BPD) is a common and serious complication of extreme prematurity. All extremely low birth weight infants (ELBW) are born before lung maturation is completed. These immature lungs are highly susceptible to damage from the aggressive resuscitation techniques that ultimately lead to their survival. Therefore, while CLD is multifactorial in origin, the use of mechanical ventilation in the immediate postpartum period is a significant predisposing factor for the condition. Just as resuscitation techniques and ventilatory strategies continue to evolve with time, so too does the nature of CLD. Periodic reassessments of the characteristics of and risk factors for the development of CLD are thus beneficial.

Objectives: A retrospective-prospective cohort study to determine risk factors for CLD in neonates born before 28 completed-weeks’ gestation.

Methods: All live-born infants born before 28 completed-weeks' gestation at Beth Israel Deaconess Medical Center between January 2004 and May 2007 were enrolled in the study. A diagnosis of CLD was made based on the need for supplemental oxygen at week 36 of corrected post-menstrual age (PMA). Immediate prepartum maternal characteristics, labor and delivery characteristics, and physiological parameters were extracted via chart review or collected through continuous data-tracking. Risk factors were analyzed using SAS software. Significance was determined based on odds ratios, logistic regression models, or the chi-square test.

Results: 198 babies were enrolled in the study between January 2004 and May 2007. Risk analyses were performed on 110 babies whose CLD diagnosis was known. Factors found to be significant for the development of CLD included birth weight (836 ± 173 g vs. 1076 ± 215 g, p<0.0001; odds ratio, 5.58, 95% CI, 1.5-20.2), gestational age at birth (26.3 ± 1.4 weeks vs. 27.6 ± 1.0 weeks, p<0.0001), early- and late-onset sepsis diagnosis (43% vs. 24%, p<0.05; and 55% vs. 23%, p<0.001, respectively), and degree of patent ductus arteriosus (PDA; 83% vs. 48%, p<0.001). While clear differences existed between the two populations of babies (those with CLD and those without) in terms of duration and degree of mechanical ventilation, these differences were found to be insignificant.
**Conclusions:** In a population of ELBW infants, risk factors for the development of CLD included gestational age, birth weight, sepsis diagnosis, and PDA. The current study did not demonstrate significance between the duration and degree of mechanical ventilation, most likely due to the study population's small size. As this is a proven risk factor for CLD, and the risk factors found in this study are largely congenital and currently beyond the control of modern medicine, clinicians should increase their efforts to minimize ventilator-induced injury in ELBW infants.

**References:**
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Tear Film Dynamics in Healthy Individuals Using a Shack-Hartmann Wavefront Sensor and Real Time Optical Coherence Tomography (OCT)

Abstract: Dry eye disease is a condition that affects an estimated 4.91 million Americans 50 years and older. Despite recent advances in the understanding of dry eye disease and treatments, there remains no single objective test for dry eye. The goal of the Dry Eye Tear Film Metrology Project at the University of Rochester is to develop new methods and clinically efficient instruments that integrate wavefront, optical coherence tomography (OCT), and ellipsometry technology to monitor tear film dynamics in vivo. The objective of this preliminary data collection project was to gather baseline data on tear film dynamics from healthy individuals using a Shack-Hartmann (SH) wavefront sensor and OCT.

Background: Tear film over the surface of the eye is important for both visual clarity and to protect the superficial structures of the eye, including the cornea and conjunctiva. In addition to water and electrolytes, tear film is a biochemical mixture consisting of mucins, immunoglobulins, antimicrobial proteins, and growth factors. Tear film dysfunction can result in a condition known as dry eye disease. The 2007 Report of the International Dry Eye Workshop (DEWS) produced the following definition for dry eye disease: "Dry Eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface." Dry eye disease is a condition that affects millions of people in the United States, including an estimated 4.91 million Americans 50 years and older. Treatment of dry eye often requires the use of medications, including eye drops and ointments.

Despite recent advances in the understanding of dry eye disease and treatments, there remains no single objective test for dry eye. In addition, there is no objective means for evaluating the efficacy of treatment. New noninvasive technology is now being used to better understand tear film dynamics.

Objectives: The objective of the Dry Eye Tear Film Metrology Project at the University of Rochester is to utilize three new technologies to evaluate tear film dynamics in real time to better understand dry eye disease. This project seeks to develop new methods and clinically efficient instruments that integrate wavefront, optical coherence tomography (OCT), and ellipsometry technology to monitor tear film dynamics in vivo. A controlled adverse environment laboratory, scheduled to be completed in 2008, will then utilize the new methods and instruments to evaluate patients for dry eye disease, monitor the effects of environmental conditions on tear film dynamics, and screen pharmaceutical agents for efficacy in treating dry eye disease.

The objective of this preliminary data collection project was to gather baseline data on tear film dynamics from healthy individuals using a Shack-Hartmann (SH) wavefront sensor and OCT.
Methods: Data was collected from individuals who did not wear contact lenses and who had no history of ocular disease. Uniform timing and blinking protocols were adhered to for all imaging procedures. Dynamic tear flow over the ocular surface was evaluated using both a SH wavefront sensor and real-time OCT.

Maximal Blink Interval (MBI) is defined by Nakamori et al. as the "longest time subjects can avoid blinking without feeling uncomfortable." Individuals participating in the project were instructed to blink rapidly three times and then voluntarily hold their eye open until they felt uncomfortable. The starting point for imaging was when an individual's eye was open after the third blink. The end point was the MBI or 15 seconds, whichever occurred first.

Shack-Hartmann (SH) Wavefront Sensor
The custom built SH wavefront sensor used in this project reflected a point source of light with a wavelength of 830nm onto the retina. Backscattered light generated an aberrated wavefront that was then relayed to a lenslet array. Wavefront measurements were captured by a SH sensor camera. A pupil camera with a topographer unit captured a simultaneous image of the tear film surface.

Real-time Optical Coherence Tomography (OCT)
The custom built OCT used in this project had a 1310 nm light source with a bandwidth of 60 nm that was connected to a telecentric optical probe. OCT uses interferometry, the superposing of two or more waves, to create two dimensional images from backscattered light when it is reflected by tissue microstructures. The technique is non-invasive and offers penetration several millimeters into a tissue with micrometer-scale resolution.

Data Analysis
SH sensor images were analyzed using the MiniWaveII program to compute Zernicke polynomials. The Fourier transform reconstructor described by Roddier and Roddier was then used to generate wavefront maps. OCT images were analyzed by a custom software program to determine the following variables: upper tear meniscus area (UTMA), upper tear meniscus radius of curvature (UTMC), upper tear meniscus height (UTMH), lower tear meniscus area (LTMA), lower tear meniscus radius of curvature (LTMC), lower tear meniscus height (LTMH), and tear film thickness (TFT).

Results: Image sequences from the pupil camera and SH sensor camera showed variability in tear film dynamics among healthy individuals. Tear film irregularities could be seen in the reflection of the topography mire of the pupil camera as "wrinkles" or "folding patterns" that increasingly distorted the concentric circles of the image. Tear film irregularities could be seen in the SH sensor camera images as "spots", "fissures", "waves," or other asymmetrical displacements of the spot pattern. The spatial and temporal patterns of tear film irregularities varied among healthy individuals. The timing of the appearance of "wrinkles" or "folding" in the pupil camera images ranged from several seconds to greater than 15 seconds.

Custom software was used to analyze image sequences from OCT to compute UTMA, UTMC, UTMH, LTMA, LTMC, LTMH, and TFT. There was no significant difference among healthy individuals for any of these variables.

Conclusions: The goal of this preliminary data collection project was to combine SH wavefront sensing and real-time OCT to study tear film dynamics. Previous studies have demonstrated the promise of using these technologies individually. However, no study has yet examined the possibility of employing both these technologies together to assess tear film on the ocular surface.
The goal of the Dry Eye Tear Film Metrology Project at the University of Rochester is to develop new methods and clinically efficient instruments that integrate wavefront, optical coherence tomography (OCT), and ellipsometry technology to monitor tear film dynamics in vivo. Under the direction of Dr. James Aquavella, Dr. Geunyoung Yoon, Dr. Shizuka Koh, and Dr. James Zavislan at the University of Rochester, collaborative projects are now underway to achieve this goal.

References
Outcomes of Subsyndromal Depression in Older Primary Care Patients

Abstract: Major depression has a point prevalence of 5-10% in older primary care patients, with considerable medical comorbidity, impact on functional status, and risk for suicide. Major depression is only the tip of the primary care iceberg, as less severe depressive conditions have even greater cumulative associated morbidity. A large number of older persons suffer clinically significant depressive symptoms that do not meet criteria for major or minor depressive disorders. We set out to study the naturalistic outcomes of elderly patients with such subsyndromal depressions (SSD). In a cohort of 745 Primary care patients age 65 years or older we found that patients with SSD differed significantly from nondepressed patients on a number of clinical scales. Three different definitions of SSD were found to have prognostic value with different subsets of patients.

Objectives: We hypothesized that patients with SSD would have worse psychopathological, medical, and functional outcomes at follow-up than non-depressed patients, but not as poor as those with minor or major depression. We also sought to explore the outcomes of three definitions of SSD to determine their relative prognostic utility.

Methods: 745 Primary care patients age 65 years or older were enlisted to undergo in-person intake interviews by a trained rater including the Structured Clinical Interview for DSM-IV (SCID) and the 24-item version of the Hamilton Rating Scale for Depression (Ham-D). Medical illness burden, basic activities of daily living, overall physical impairments, and components of executive functioning were also measured. Similar in-person follow-up interviews were completed at one year. Patients were grouped for analysis based on depression diagnosis into major depressed, minor depressed, SSD, or non-depressed categories. Three different definitions of SSD were used based on previous works, each representing a unique set of patients.

Results: All three definitions of SSD predicted outcomes at one year that were significantly different from the non-depressed group. Which outcomes were different depended on the definition used.

Conclusions: Subsyndromal depression is a useful category for predicting poor outcomes in patients that do not meet the criteria for minor depression. Researchers might choose their approach to SSD definition based on the outcomes of interest.

References:

Assessing the Impact of Vaccine Discussion Groups on HIV-1 Vaccine Knowledge and Attitudes

Abstract: Finding an effective HIV vaccine could dramatically reduce transmission of HIV-1. There are many HIV-1 vaccine trials currently being conducted worldwide in areas of high HIV-1 prevalence. Participant understanding of the vaccine trials and informed consent are critical components to conducting valid, complete studies. Prior to enrollment in the HIV Vaccine Trial Network (HVTN) protocol #503N, volunteers must attend a series of two HIV-1 education sessions called Vaccine Discussion Groups (VDGs). VDGs teach prospective vaccine trial volunteers about HIV-1 infection, the role of vaccines in preventing disease, and protocols specific to HIV-1 vaccine trials. This study evaluates the effectiveness of the two-session VDG program of the HVTN 503N protocol in Cape Town, South Africa, in educating prospective HIV-1 vaccine trial participants about HIV-1 and HIV-1 vaccines.

Objectives: The purpose of this study is to evaluate the effectiveness of Vaccine Discussion Groups (VDGs).

Methods: A self-administered 19-question survey was distributed to VDG participants at three time points: 1) before the first VDG session (pre-VDG-1), 2) after the first VDG session (post-VDG-1), and 3) after the second VDG session (post-VDG-2). The survey included questions regarding general baseline HIV-1 knowledge, knowledge about vaccines, knowledge about HIV-1 vaccine trials, and personal attitudes towards HIV-1. The general baseline knowledge questions (seven questions in addition to the standard 19 questions asked at every time point) were administered at pre-VDG-1, before any VDG sessions were taught. T-tests and paired T-tests were used to analyze survey results with significance set at p<0.05.

Results:

Baseline knowledge questions
The mean score for the seven baseline knowledge questions administered at pre-VDG-1 was 83%, with a median score of 86% (6 out of 7 answers correct). Participants that received a high school education or beyond scored 12% and 13% higher, respectively, on the baseline HIV-1 knowledge questions than those that received a primary school education (p=0.02, p=0.04). Having a sex partner also significantly increased one's baseline knowledge score (p=0.003).

HIV-1 vaccine and HIV-1 vaccine trial knowledge questions
Participants answered more HIV-1 vaccine and HIV-1 vaccine trial knowledge questions correctly at post-VDG-2 than at post-VDG-1 (p=0.0036) or pre-VDG-1 (p=0.0002). There were no significant differences in correctly answered knowledge questions between pre-VDG-1 and post-VDG-1 (p=0.40).
Attitudes towards HIV-1
32% of participants believed that HIV-1 in their community had affected their lives. 35% felt they could be at risk for contracting HIV-1. 19% wanted an HIV-1 positive test result to remain a secret. 59% of participants claimed that they would join an HIV-1 vaccine trial.

Conclusions: VDGs are effective at increasing knowledge about HIV-1, HIV-1 vaccines, and HIV-1 vaccine trials after two VDG sessions, but not significantly effective after only the first VDG session. The results of this study can be followed-up through further studies that examine HIV-1 knowledge and attitudes in the Nyanga community outside of the vaccine trial discussion groups.

References:
1) UNAIDS, WHO. AIDS epidemic update. 2004; UNAIDS/04.45E.
2) UNAIDS. Report on the global HIV/AIDS epidemic. 2003; UNAIDS/03.39E.
Basic Science and Clinical Research

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Preceptor:
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Synergistic Toxicities Affect Osteoblast Activity - A Paradigm for Accelerated Bone Loss in Osteoporosis

Objective: It has been estimated that nearly 28 million people in the United States suffer from osteoporosis or are at risk for the condition. A decrease in activity of the predominant cell for bone growth, the osteoblast, hastens the onset of osteoporosis. Within the osteoblast, a protein has been characterized (the aryl hydrocarbon receptor - AHR) that has been implicated in mediating the toxic effects of cigarette smoke on endocrine disruption, cell differentiation and tumor promotion in other cell types. In addition, it has been demonstrated that over 95% of the body's lead (Pb) burden is stored in bone, further depressing the activity of osteoblasts. Preliminary studies indicated a strong adverse interrelationship between cigarette smoking and lead exposure on osteoblast function. The objectives of this study were to determine if lead increased the expression of AHR in osteoblasts and to investigate the effects on proliferation in lead exposed osteoblasts subjected to a cigarette smoke extract ligand.

Methods: Two distinct osteoblast cell lines were cultured, one for lead exposure and one for control, to determine the effect of lead on AHR expression via Western blot analysis. The lead exposed cells were subjected to a cigarette smoke extract ligand to investigate the collective effect on osteoblast proliferation using BRDU labeling assay.

Results: At the time of writing, further laboratory studies are being conducted and interpreted and data collection is still in progress.

Conclusion: For a full interpretation of the results of this study please see the poster presentation.
Abstract: Tactile deficits, and their related complications, are alarmingly prevalent in certain clinical populations, notably diabetic patients, stroke survivors, and the elderly. For diabetic patients, years of systemic glucose imbalance often leads to peripheral neuropathy, a condition that can result in marked numbness of the extremities (Adler et al. 1997; Abbott et al. 1998) leading to serious medical problems like skin ulcers, skeletal pathologies such as Charcot’s joints (Serra et al. 1997) and in severe cases it becomes necessary to amputate the affected extremity. A wide range of studies in a variety of systems-including global climates, radio frequency communication, and sensory neurons-have shown that the presence of certain kinds of noise, whether audio or visual can actually enhance information transmission. These IRB-approved studies have shown conclusively that this "stochastic resonance" significantly lowers the threshold of sensation of tactile and proprioceptive systems (Collins et al. 1996; Cordo et al. 1996; Collins et al. 1997; Richardson et al. 1998). Interestingly, they have established that both electrical and mechanical modalities of noise increase sensitivity. This study focuses on mechanical noise.

Objectives: The purpose of this project is to investigate how tactile sensitivity is affected by mechanical vibration delivered to the plantar surface of the foot. This is a Phase II project supported by the NIDDK at the NIH. In our Phase I program, using similar methods and procedures, we demonstrated that subsensory noise could enhance the tactile sensitivity of subjects who experience peripheral neuropathy as a result of diabetes. In addition, these improvements could be measured using standard clinical examinations used to assess In this Phase II study, we will try to establish an optimal stimulation that can be tailored to the individual subject, as well as examine any adaptation effects when the stimulation is used for moderate intervals in a confined experimental setting.

Methods: We drew subjects from the diabetic population of individuals with known diminished peripheral sensation. We used clinically accepted techniques for determining sensitivity. The mechanical vibration was applied using a boot apparatus containing a vibrating insole. We were able to manipulate the level of vibration to a level just below the subjects' threshold of sensation. The first part of the study measured changed in sensitivity following mechanical stimulation of the foot. A second part of the study measured the adaptation of the subject to the stimulation, specifically does the effect of the stimulation change after one hour of continuous application.

Results: The data collection has been completed but results are pending, although preliminary data has been very encouraging.
References


Pain Treatment in a Pediatric Emergency Department: Associations with Pain Scores Following Implementation of Mandatory Pain Score Documentation Requirements

Objectives: Treatment of pain in Pediatric Emergency Department (ED) patients is an important measure of quality care. Pain score documentation has been proposed as a means to improve pain management. In light of existing research showing low rates of documentation, in 2001 the Joint Commission mandated pain score documentation.¹ This study aimed to examine the relationship between pain score documentation and analgesia administration among pediatric ED patients.

Methods: A secondary analysis of existing research data was conducted. The data were collected in a large, urban, academic medical center ED. Patients were randomly selected prospectively over a 15-month period in 2005-2006, and trained research nurses reviewed the ED medical record to abstract demographic information, pain scores, analgesic medications administered, and times. Follow up pain scores were defined as those documented within 2 hours of the initial pain score. Descriptive and chi square statistics were calculated.

Results: 4,721 patients were enrolled. An initial pain score was documented in 87% of patients. Patients with a pain score recorded were significantly more likely to receive an analgesic (38% vs. 30%, p<0.001), and to receive a second dose (7.6% vs. 4.3%, p=0.004). Only 47% of patients with an initial score ≥7110 received any analgesic, with patients under 8 having the lowest treatment rates (36.8% vs. 58% for patients over 8, p<0.001). IV opioids were administered to 12.9% of patients with initial scores ≥7, but to only 1.8% of patients with initial scores <7 (p<0.001). Follow up pain scores were documented in only 18% of patients with initial pain scores ≥7. Patients with follow up pain score documentation were three times more likely to receive a second dose of analgesia (p<0.001). Conclusions: In this pediatric population, initial pain score documentation was common and was associated with analgesia use. Despite a high rate of initial pain score documentation, overall analgesic administration was suboptimal. Follow up pain score documentation was infrequent but was associated with further dosing of analgesics, possibly indicating that increased documentation is associated with a higher quality of pain management. More research is needed to determine whether there is a causal relationship between the acquisition of pain scores and the treatment of pain.

References:
Three Generations of Recovery: War and Malaria

Objectives:
In order to examine the question of how a community is able to recover in the wake of tragedy, this study examines the viewpoints of three generations from a community that was traumatically affected by malaria as a direct result of war.

Background, Justification of Research site:
This study concerns the geographic area of Ishigaki Island at the very tip of present day Okinawa Prefecture. During the last months of the Pacific War (June -August 1945) in the face of feared invasion, local inhabitants were evacuated from their homes to makeshift shelters and caves in the undeveloped interior. Due to this evacuation, along with concurrent malnutrition and starvation, over half the population was infected with malaria. Eventual fatalities were around 25% of those infected, with the old and young hit the hardest.

Methods:
This study utilized interviews from three generations: war-time survivors, the immediate post-war generation, and people currently in their twenties and early thirties. Observations made on-site at memorial services, schools, museums and municipal centers of government in Ishigaki as well as in Naha, Okinawa were also used.

Results/Conclusions:
The data shows that the local government has made an effort to promote the wartime malaria epidemic as both a political tool and also as a means to spread a general message on the horrors of war. Though knowledge of the events, as well as personal strength of feeling fall precipitously with each younger generation, all groups associate the memory of the wartime past with an understanding and desire to work for peace in the future.
The Robotic Radical Cystectomy: Outcomes and Efficacy

Introduction: While open radical cystectomy remains the gold standard for the treatment of muscle invasive bladder cancer, the continued refinement of laparoscopic techniques and the success of robotic assistance in radical prostatectomy have led to great interest in extending a minimally invasive approach to bladder cancer. We report our initial experience with robotic-assisted laparoscopic radical cystectomy for benign and malignant disease describing stepwise the surgical procedure and evaluating perioperative and pathologic outcomes of this procedure.

Methods: Over fifty patients underwent robotic-assisted laparoscopic radical cystectomy with various urinary diversions for clinically localized bladder cancer. The stepwise operative procedure is described in detail and shown in the video. Outcome measures evaluated included operative variables, hospital recovery, pathologic outcomes, and complication rate.

Results: We have performed over 50 robotic cystectomies at our center to date. 26 patients had sufficient follow-up for analysis (> 1 year). There were 22 males and 4 females that had an operation. Mean age was 65 yr (range: 38-86 yr). Average BMI was 27.6 with a range between 20-38. Over 90% of patients presented with hematuria and the major pathologic entity warranting cystectomy was TCC (TCC in 22 patients; urachal anomalies/carcinoma in 3; and 1 patient had a neurogenic bladder). The average OR time was 5.5 hours with a range (4-8.5 hours including the urinary diversion). Mean estimated blood loss was 214cc (100-500cc). The majority of patients has ileal loop diversion (n=20), while 4 patients had neobladders and 2 having Indiana pouches. In most cases the urinary diversion was performed extracorporeally. On surgical pathology, 22 patients had TCC with 14 patients having Tis or <=pT2, 6 patients pT3, and 2 patients T4 disease. In no case was there inadvertent entry into the bladder during surgery. Our positive surgical margin was 14% and lymph nodes were positive in 27% of patients. Lymph Node count increased with every 10 cases. There was no transfusions and the average hospital stay was 10days (4-25d). The most common post-operative complication was UTI; other complications included ARF (1), anastamotic leak (1), prolonged ileus (4) and DVT (1).

Conclusions: Our initial experience with robotic-assisted laparoscopic radical cystectomy appears to be favorable with acceptable operative, pathologic, and short-term clinical outcomes. As our experience increases, we should expect to continue to refine our surgical technique and reduce operating room times. Larger experiences are required to adequately evaluate and validate this procedure as an appropriate surgical and oncologic option for the bladder cancer patient.
Abstract: Potential treatment strategies for both acute and chronic liver failure, as well as inherited metabolic disorders include transplantation of fetal liver cells. Homogenous liver samples possess hepatocytes, kupffer cells, and erythropoietic precursors, which may be useful for transplantation. In the past, HLA II but not HLA I (A, B, C) characteristics have been elucidated on human fetal liver cells. Immature human fetal hepatocytes may show low expression of Major Histocompatibility (MHC) antigens or immunosuppressive surface molecules. Immature cells generally possess low immunogenicity, but this characteristic has not been investigated on human fetal hepatocytes. Additionally, human fetal hepatocytes may express HLA-G, which has an immunosuppressive effect.

Objectives: The aim is to determine if human fetal hepatocytes possess immunological advantages which may be beneficial for hepatocyte transplantation.

Methods: Previously acquired fetal liver samples will be characterized using three techniques – flow cytometry, molecular biology, and serology. A flow cytometer will be used to investigate pan-HLA class I antigen expression. Analysis of gene expression will be determined using HLA molecular analysis after DNA/RNA extraction, PCR, and gel electrophoresis for HLA class I and II. Standard serologic techniques using Terasaki trays will be used for HLA I typing.

Results: Pending

Conclusions: Pending
The Effect of LRPII Cluster Administration on Brain AP Levels in an Older AD Mouse Model

Abstract
Amyloid-P peptide (AP) accumulation in brain contributes to the onset of Alzheimer's Disease (AD). Dysfunction in AP clearance leads to excess AP in the brain and plays an important role in AD pathogenesis. Low-density lipoprotein receptor related protein 1 (LRP1) is the main transporter involved in AP clearance from the brain. LRPII contains four ligand binding domains (LRPI, II, III, and IV clusters) and it has been shown that LRPII and IV bind AP with high affinity. LRPII and IV, when administered intravenously into AD mouse models, sequester plasma AP and reduce brain AP levels. In this study, a triple transgenic mouse AD model (3Tg) was used. These 3Tg mice (aged 11-14 months) were given LRPII intravenously as a bolus and blood samples were collected before injection, at 6 hours, and at 12 hours. At 12 hours CSF, hippocampus, and cerebral cortex were collected. AP levels were measured in plasma, brain, and CSF by ELISA and showed no significant change. Brain capillaries were isolated and LRPI levels measured in 6 and 11 month old 3Tg mice by Western blot analysis, which showed a decrease in LRPII levels in the older mice. These results indicate that AP efflux across Blood-Brain Barrier (BBB) may be limited in older mice due to decreased LRPI in brain microvessels. This may explain the lack of significant changes in brain AP levels in LRPII treated mice. Further work is needed with a larger number of mice to determine if these findings are significant.

Aims:
The purpose of this study was to investigate whether introducing LRPII (which does not cross BBB) in 11-14 month old 3Tg-AD mice would sequester AP in plasma and clear AP from brain. We hypothesized that introducing LRPII would increase plasma AP levels and decrease AP levels in the brain and CSF.

Materials and Methods
Animals: 3Tg AD (PS1ml46v, APPswe, TauP301L) mice (Oddo et al., 2003) obtained from Dr. Frank LaFerla, University of California, Irvine.
LRPII: Recombinant LRP fragments encompassing cluster II were produced using stable transfected baby hamster kidney cell lines (Weinstein et al., 2002).
Route of Administration and Sample Collection: Mice (11-14 months old) were given either a single bolus of 20µg LRPII or saline (control) via the femoral vein and blood samples were collected at pre, 6 and 12 hrs after the injection.
At the end of the experiment CSF samples were collected from the cisterna magna. Brain samples were also collected and divided into hippocampal and cortical portions.
Brain capillary isolation Brain capillaries were isolated from untreated 3Tg mice aged 6 and 10 months for quantification of LRPI and RAGE levels by Western Blot analysis.
ELISA: Plasma, brain, and CSF levels of human A1340 and 42 were quantified by sandwich ELISA kit (Biosource International., Camarillo, CA).
Western Blot Antibodies:
LRPL- LRP-85 monoclonal mouse antibody against C-terminal domain of human LRPL -chain, which cross reacts with mouse LRPL (5A6, 1:1000, 1µg/ml, EMD Biosciences, Inc., San diego, CA).
RAGE- rat monoclonal antibody against mouse/rat RAGE (MAB 1179, 1:1000, 1µg/ml, R&D systems Inc., Minneapolis, ME).
Actin- goat polyclonal IgG against C-terminus of human actin, which cross reacts with mouse actin (I-19, sc-1616, 1:1000, 0.2µg/ml, Santa Cruz Biotech., Inc., Santa Cruza, CA).

Results:
- Although some change across time could be observed in plasma Al340 levels of treated mice, this change was not significant (figure 2).
- Plasma Al342 levels remained low after treatment and there was no significant difference between treated and control groups at 12 hours (figure 3).
- Similarly, brain and CSF A1340 and 42 levels did not show a significant change 12 hours after injection (figures 4-6).
- LRPL levels were reduced in 11 month old mice when compared to 6 month old mice (figures 7 and 8).
- RAGE levels were increased in 11 month old mice when compared to 6 moth old mice (figures 7 and 8).

Conclusions:
- The Western blot in this study in conjunction with the minor changes seen in plasma and brain suggest that Al3 efflux in older 3Tg mice may be impaired due to low LRPL levels in brain capillaries.
- An increase in RAGE in brain capillaries may also play a role in dysfunctional Al3 clearance in older mice.
- Caution should be used in interpreting these results until they can be reproduced in a larger number of mice.
- Future directions include immunostaining brain sections for Al340 and 42 levels to confirm the ELISA results of this study.

References:
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**Neuronal Activation in Differentially Handled C57BL/6 Male Mice Subject to Acoustic Stress**

**Abstract:**
Recent research has demonstrated the value of early gene products such as c-fos proteins as powerful markers of neuroendocrine activation in brains of stressed rodents. Particularly, c-fos activation patterns in acoustically stressed animals have been cited as a method to explore the intricate and often elusive inter-relationships of neuroanatomical structures involved in the hypothalamic-pituitary-adrenal (HPA) axis and classic stress response. This study utilized four differentially handled experimental C57BL/6-mice groups in order to study the neuronal activation response to acoustic stress via c-fos in situ hybridization and subsequent radiographic imaging studies. Brain regions analyzed included the paraventricular nucleus (PVN) of the hypothalamus, lateral septum, cingulate cortex, and the hippocampal formation, specifically the dentate gyrus and cornu ammonis fields (CA1/CA2 and CA3). All of the aforementioned structures play a critical role in an animal's neuroendocrine and behavioral response to stress and display stress-induced c-fos activation. The PVN is a major hypothalamic nucleus involved in the regulation of pituitary hormone release during periods of stress whereas the hippocampal formation is involved in memory incorporation and fear responses as it is highly interconnected with the limbic system. Both the lateral septum and cingulate cortex demonstrate higher-level, cortical processing of stress and also possess significant limbic connections. The study holds great import since studies of stress-induced c-fos mRNA patterns in differentially handled mice have never been attempted. Findings from experimentation can contribute to the current knowledge base of developmental research.

**Objectives:**
The primary objective of this study was to determine what significant differences, if any, existed between various experimental groups in regard to both quantity and pattern of neuronal activation elicited by an acoustic stressor. Outcomes such as differences in levels of circulating plasma cortisol in experimental groups have also been a subject of exploration based on this study.

**Methods:**
This study utilized an acoustic stressor paradigm involving four experimental groups of six C57BL/6 male mice which underwent various handling protocols prior to acoustic stress exposure: group housed, no stress (GHNS, TO); group housed, individually stressed (GHSA, T30); group housed, group stressed (GHGS, T30); and twenty-four hour isolated, individually stressed animals (24Iso, TO and T30). All animals were obtained from Charles River Laboratories, NC and placed four per polycarbonate housing cage upon arrival to the research laboratory. Animals received food and water ad libitum and were exposed to 12:12 light-dark cycle conditions. After approximately two weeks of environmental acclimation, mice from the respective experimental groups underwent acoustic stress testing involving exposure to 15 minutes of 100 dB white noise in a sound-attenuating chamber.
The group housed, no stress (GHNS) group received no acoustic stress and served as a control for the study. Animals of the group housed, group stressed (GHGS) group were not handled prior to experimentation and remained in their respective cages for testing. In contrast, the group housed, stressed alone (GHSA) animals were removed from group cages immediately prior to testing and placed in individual cages. The 24 hour isolated (24 Iso) group again was handled and separated into individual cages prior to experimentation as the group housed, stressed alone (GHSA) group but separation occurred approximately 24 hours before stress testing took place. Experimental animals were decapitated at time 0 (TO) minutes into the stress protocol (GHNS, TO; 24 Isa, TO) or time 30 (T30) minutes (GHGS, T30; GHSA, T30; 24 Iso, T30). Thus, the 24 hour isolated TO group also served as an additional control in the study. Blood samples were obtained at the time of decapitation in order to measure circulating levels of plasma cortisol.

Extracted brains were postfixed and cut coronally into 12 µm sections using a cryostat. Brain sections were then mounted to Superfrost plus slides with a total of six sections placed per slide. Slides were stored in a -80°C freezer to await further processing via in situ hybridization.

In Situ Hybridization: In situ hybridization of brains was carried out to radioactively label c-fos mRNA in sections of mouse brain tissue. Selected representative slides were incubated with S35 labeled antisense c-fos mRNA riboprobe according to previously described in situ hybridization techniques.3

Radiographic studies: Slides were exposed to radiographic film for four days in order to visualize radioactively tagged c-fos mRNA. Developed radiographic images were digitally photographed using a light box and Panasonic CCTV camera with a Navitar macro zoom 18-108 F/2.5 lens. All images were captured in one sitting using the same ambient light level. The index of neuronal activation as expressed by presence of c-fos mRNA was quantified by implementing the Scion Image® software to determine the average optical density of captured coronal brain sections. A positive optical density signal was considered to be 3.5 standard deviations above the mean background optical density of sections. Sections or structures containing greater optical density measurements were presumed to have a more active neuronal activity level as evidenced by increased transcription of c-fos DNA elements into c-fos messenger RNA. C-fos messenger RNA was considered an accurate gauge of short-term changes in neurons since formation and processing of Fos proteins requires a significantly longer time period and may not be reflective of relatively brief fluctuations in neuronal activation.

Statistical analysis: All sections containing structures of interest were analyzed and the six highest optical density values of each animal were averaged to yield a single value per animal. StatView® statistical software was employed to graph and statistically analyze data. A two-way analysis of variance and a Fisher's pairwise least significant post hoc test were conducted to detect significant differences in the dataset.

Results:

Statistical analysis of data allowed several conclusions to be drawn regarding the study. It is important to note that every brain region analyzed (PVN, lateral septum, cingulate cortex, dentate gyrus, CA1/CA2 and CA3 fields) demonstrated a significant overall ANOVA result (p<0.05). Furthermore, brains of stressed animals (T30 groups) showed a level of neuronal activation greater than that of control, TO groups in every structural analysis. A consistent neuronal activation trend was observed in the PVN, cingulate cortex, dentate gyrus and CA fields in which group housed, stressed alone (GHSA) animals demonstrated the greatest optical densities, followed by group housed, group stressed (GHGS) and 24 hour isolated (24 Iso, T30) with both control groups (GHNS, TO; 24 Iso, TO) showing the lowest optical densities. The only notable exception to this trend occurred in the lateral septum, where the group housed, group stressed (GHGS) brains had the greatest optical density measurements. Although these trends suggest an overall patterning of stress induced c-jos activation, tremendous variability existed between groups in Fisher's PLSD. Analysis of data in this study is ongoing as more brain regions are being captured and analyzed.
References


LRP-11 Cluster Administration Reduces Brain Aβ in Younger Triple Transgenic AD Mice

**Background:** Accumulation of amyloid (3-peptide (Aβ)) in the brain is a significant contributor to the development of Alzheimer's Disease (AD). At critical concentrations, Aβ forms insoluble plaques in the brain tissue, which initiates a pathogenic cascade of events that ultimately result in neuronal toxicity and neurodegeneration (Hardy et al., 2002). Low-density lipoprotein-related receptor protein (LRP)-1 is the main transporter in the brain capillary endothelium that moves Aβ from brain to plasma. It possesses four ligand binding clusters (LRP-1 to LRP-IV). Clusters II and IV bind with high affinity to Aβ, particularly Aβ40 (Kd =0.6-1.2 nM) (Deane et al., 2004).

**Objective:** The purpose of this study was to examine the efficacy of soluble LRP-11 as an Aβ sequestering agent to prevent the accumulation of Aβ in the brain of young triple-transgenic AD model mice (3Tg-AD). We hypothesized that administration of soluble LRP-II would bind and sequester free plasma Aβ to create a concentration gradient favoring the efflux of brain Aβ, as well as, block Aβ entry into brain; thus, increasing levels of plasma Aβ, while lowering levels of brain Aβ.

**Methods:** 6-7 month old 3Tg-AD (PS1M146V, APPswe, and tauP301L) model mice (Oddo et al., 2003) were administered either 20µg of LRP-II or SOµL of saline through a rapid intravenous injection. Plasma samples were collected prior to injection, and 6hrs and 12hrs post injection. After 12hrs, CSF, hippocampus, and cortex were collected. Levels of human Aβ40 and Aβ42 in all plasma, CSF, hippocampus, and cortex samples were quantified by sandwich ELISA. Brain capillaries were isolated and analyzed via Western Blot to quantify the amount of LRP-1 present in the endothelium of 3Tg-AD mice.

**Results:** The results demonstrated that LRP-II administration diminished Aβ40 and Aβ42 in the CSF and in hippocampus, as well as decreased Aβ42 in cortex compared to age-matched controls. The plasma levels of Aβ40 and Aβ42 in the LRP-11 treated group were increased compared to controls, with the increase peeking 6hrs post-injection.

**Conclusions:** While these results were not significant there is a clear trend showing that LRP-11 creates a gradient favoring the efflux of Aβ from brain to plasma across the blood-brain barrier, and that LRP-1 levels in the capillary endothelium permit rapid export of Aβ from brain. Further studies using a larger sample size is necessary to ascertain the maximum potential of LRP-II in preventing accumulation of Aβ in the brain, and thus its potential to alter the development of Alzheimer’s Disease.

**References:**
Deane, Rashid, Zhenhua Wu, Abbay Sagare, Judianne Davis, Shi Du Yan, Katie Hamm, Feng Xu,


Plasmacytoid Dendritic Cells in Ocular Rosacea and Ocular Cicatricial Pemphigoid

Abstract:
Acne rosacea is a common but little-known chronic disease of the facial skin that affects an estimated 14 million Americans. The cause of the disease is unknown, but it is characterized by vascular dilation of the central face, with redness, papules, and pustules appearing over the nose, cheeks, eyelids, and forehead. In a significant percentage of patients there is also severe ocular involvement, including foreign body sensation, burning, telangiectasia (dilation of small vessels) and irregularity of lid margins, meibomian gland dysfunction, blepharitis, and conjunctivitis. Earlier histologic and immunopathologic studies of rosacea attempted to identify and categorize the chronic inflammatory cells present in conjunctiva and substantia propria affected by the disease, but no study has examined diseased conjunctiva for the presence of plasmacytoid dendritic cells (PDCs), a subset of antigen-presenting cells that produce large amounts of interferon-alpha, and mediate inflammatory reactions in pathologic processes affecting muscle, lung, and conjunctivae. The specific aim of this project is to investigate conjunctiva affected by rosacea for the presence of plasmacytoid dendritic cells through the use of immunohistochemical staining techniques with a panel of antibodies specific to cell surface markers on PDCs: CD123, IL-12, and TLR9. Conjunctiva affected by rosacea were compared to stains of normal conjunctiva and conjunctiva inflamed by a different disease process, ocular cicatricial pemphigoid. Unfortunately, the results of the experiment were difficult to interpret due to enhanced staining of primary controls with the avidin-biotin complex method of immunohistochemistry. Various strategies employed to resolve this dilemma yielded only minimal improvement such that it is impossible to say, based on this project, whether or not PDCs are present in ocular rosacea or ocular cicatricial pemphigoid.

Objectives:
To examine whether plasmacytoid dendritic cells (PDCs) are constituents of the inflammatory process affecting conjunctiva in patients with ocular rosacea and ocular cicatricial pemphigoid.

Methods:
Inflamed conjunctivae biopsied from rosacea patients, ocular cicatricial pemphigoid patients, and normal patients were placed in phosphate-buffered saline (PBS), pH 7.2, snap-frozen, and embedded in OCT compound. Four micron cryosections were mounted on gelatin-coated slides for immunoperoxidase studies (avidin-biotin complex staining). Each experiment consisted of two slides, the test slide, with three different dilutions of the primary antibody (6 wells total), and the control slide, which had two wells each of three different controls: (1) without primary antibody, (2) without secondary antibody (biotinylated), and (3) collagen IV.
Slides were removed from -80°C refrigerator and allowed to air dry for 10 minutes. Next, slides were placed in cold acetone for 10 minutes, then the slides were removed and each tissue section was blocked with 25 ul diluted (1/10) normal mouse serum, or goat serum for the collagen IV control, and incubated in a moist chamber for 30 minutes. The slides were then blocked with 25 ul mouse anti-human primary antibody (specific to PDC surface markers) at varying dilution concentrations of III00, 1/50, and...
1/25, and incubated for one hour in the moist chamber. After the incubation, the slides were rinsed in 1% BSA-PBS for 3 minutes, and this rinse was repeated three times. Next, the tissue was blocked with 25 ul diluted (1/20) normal goat serum (rabbit for collagen IV) and incubated in the chamber for 30 minutes. Afterward, the slides were blocked with 25 ul diluted (1/1500) biotinylated goat anti-mouse IgG placed in each well, and were incubated for 1 hour. The slides were removed from the incubation chamber and rinsed in 1% BSA-PBS as above. Next, the slides were blocked by adding 25 ul ABC Kit (1 drop orange dye and 1 drop brown dye in 2.5 ml of 1% BSA-PBS) to each tissue well and incubating for 30 minutes. Next, the DAB Kit SK-4100 solution was prepared by adding 1 drop stock buffer, 2 drops DAB, and 1 drop hydrogen peroxide to 2.5 ml distilled water. The slides were removed from the incubation chamber, the DAB substrate was added to each well, and the reaction was then viewed under the microscope. When the cell membrane turned brown, the slide was removed from the microscope and washed in distilled water. Each slide was stained in this manner. Next, the slides were counterstained with Histostik, or Gill's Formula Hematoxylin, for 20 seconds and then placed back in distilled water. Lastly, the slides were mounted with alcohol washes (70% for 5 minutes, 80% for 5 minutes, 95% for 5 minutes, 100% for 5 minutes), xylene, and Crystal mount.

Results:
Immunohistochemical staining with the avidin-biotin complex method produced ambiguous results. Staining of rosacea and ocular cicatrical pemphigoid showed some stromal and nuclear positivity for CD123, a cell surface receptor specific to PDCs; however, normal conjunctiva taken from patients undergoing cataract surgery also displayed similar staining patterns. Therefore, this positive staining pattern, though possibly significant, could not be interpreted as such because of the lack of good controls in normal patients. Also, the controls in which primary antibody was not added showed a high-degree of staining that proved to be very characteristic of this method, but which made the interpretation of the experimental slide difficult because all cells showed this odd staining, including cells that were negative on experimental slides.

In an attempt to obtain better staining results, we tried a number of different procedures, including altering the incubation time periods, altering the dilution levels of the various reagents, and blocking the slides twice with normal serum to better remove any artifacts and improve the staining background. None of these attempted improvements produced better results.

Conclusions:
Since the primary controls showed unexpected positive staining, it was impossible to say whether or not PDCs were present in the diseased conjunctiva. There did appear to be some positive staining, especially with CD123 and TLR9; however, before these results can be interpreted, the procedure must be improved so that the controls show more appropriate levels of staining and allow comparisons to be made with the experimental slides.

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Abstract:
RNA is becoming an important therapeutic target. Increasingly, RNA molecules have been identified as playing essential roles in various pathogenesis. For example, the bacteriophage phi 29 depends on an RNA molecule for the proper packaging of the viral genome into the assembling capsid. This mechanism is believed to be conserved across several different types of viruses, including human viruses. This project will attempt to cause misfolding of the native phi 29 packaging RNA by stabilizing predicted sub-optimal secondary structures using sequence specific oligonucleotide binding. The ability of the infected bacteria to produce viable bacteriophage will be assessed after oligonucleotide treatment to determine if misfolding of packaging RNA inhibits the assembly of mature phi 29 virus.

Objectives:
To express a small RNA molecule in *B. subtilis* that will disrupt the replication cycle of bacteriophage phi 29 by inducing misfolding of a viral RNA essential for genome packaging.

Methods:
An insert was designed that codes for a small RNA molecule complementary to a region of bacteriophage phi 29's packaging RNA. This insert was incorporated into the MCS of shuttle vector pH201 using BAMHI and ECORI restriction sites. Transformation of *B. subtilis* will be conducted using standard electroporation procedures. Transformed and control samples will be grown with bacteriophage phi 29 in liquid media overnight. The amount of viable phage particles in each sample will be assessed using a plaque forming assay.

Results:
The coding insert was successfully incorporated into the MCS of shuttle vector pH201. Agarose gel electrophoresis analysis was used to confirm appropriate vector size. Further data collection will begin upon receipt of bacteriophage phi 29 samples.

Conclusions:
Pending further investigation

References
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Predicting Sedation Induced Respiratory Compromise during Colonoscopy

Introduction: Predicting respiratory compromise during sedation for colonoscopies is beneficial as more patients are presenting with Obstructive Sleep Apnea (OSA). Given that the majority of respiratory events that occur during sedation are the result of upper airway collapse (UAC), and given that sleep apnea patients exhibit UAC without sedation, it seems likely that these factors would interact to produce added risk. Measurement of upper airway collapsibility offers potential in assessing the propensity for sedatives to produce airway obstruction. The specific aim for this study was to compare the propensity for upper airway collapsibility during sedation (as provoked by a negative airway pressure challenge) to the need for clinical intervention to maintain adequate ventilation during colonoscopy.

Methods: We recruited patients, ages 18-80, of any gender or race who were scheduled for outpatient colonoscopy under intravenous sedation with one gastroenterologist. Patients with OSA were excluded from this study. All subjects were also monitored with modified polysomnography for characterization of sleep and sedation patterns. The two primary outcomes were upper airway collapsibility and the degree of clinical intervention.

Results: Twenty subjects (7 female) completed the study. A level of mild-moderate intravenous sedation was accomplished with the combination of a benzodiazepine (midazolam) and opioid (meperidine (n=18), fentanyl (n=2)), and the occasional use of an antihistamine (diphenhydramine (n=3)). The tendency towards upper airway collapse depended on the presence of sleep co-existing with sedation. When sleep occurred during sedation, less negative airway pressure was required in order to destabilize the airway than when the patient was electroencephalographically awake. Interestingly, the prevalence of sleep in this cohort was similar during the immediate-post colonoscopy interval and just prior to discharge, and was less so when the patient was deemed adequately sedated by the gastroenterologist and ready to begin the colonoscopy.

Conclusions: The interaction of sleep and sedation potentiated the occurrence of respiratory instability in this cohort. The occurrence of upper airway flow limitation as provoked by the application of negative airway pressure did not predict the need for clinical intervention (CIS) to restore adequate ventilation during colonoscopies. However, the CIS was quantified during a period of intense stimulation and may not represent the true vulnerability of sedated patients to respiratory morbidity. This is underscored by the prevalence of sleepiness in this cohort just prior to discharge and the collapsibility of the upper airway even during this breathing run. These findings support previous studies that determined the importance of a wakefulness drive to maintain adequate ventilation. Sleep and sedation put the individual at risk for hypoxemia from adverse respiratory events. Presumably, the common risk exists because both alter respiratory drive and upper airway tone. As many sedatives and opioid analgesics are direct respiratory depressants -and sleep itself is a risk factor for UAC, it is imperative to appreciate the synergy of sleep and sedation in causing respiratory compromise.
Basic Science and Clinical Research

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Pandemic Influenza: Antiviral Preparedness and Healthcare Workers

Abstract:
The threat of an influenza pandemic is constant and the occurrence of one virtually inevitable. A novel influenza virus could spread worldwide and produce devastating effects. The impact of pandemics is substantial but can be mitigated through preparedness. One significant component of an obviously multi-faceted plan is the use of antiviral agents, which the World Health Organization recommends stockpiling.

Objectives: The purpose of this study was twofold: first, to justify the need for institutional stockpiling of the preferred antiviral agent as an effective component of pandemic preparedness and second, to determine the preparedness of hospitals in the Finger Lakes Region (FLR).

Methods: I performed an extensive primary literature search and examined relevant government publications. A survey of the 17 FLR hospitals was conducted via e-mail. They were asked the following questions:
1) What are your hospital's par levels for amantadine, rimantadine, oseltamivir (Tamiflu), and zanamivir (Relenza)?
2) How many courses of the above are stockpiled?
3) What is the total number of personnel (medical and non-medical staff) with patient contact?
4) How many of the above personnel received influenza vaccination through the hospital?
Clarifications were made via e-mail as well.

Results: Antivirals will be in particularly high demand during the beginning of a pandemic before an effective vaccine is available. Because the manufacturing time of neuraminidase inhibitors, such as oseltamivir and zanamivir, is lengthy and there is limited surge capacity, manufacturers would not be able to keep up with demand. Oseltamivir is the best choice for stockpiling given its safety profile, association with reduction in secondary complications, and predicted efficacy against pandemic viruses as well as the low-level of oseltamivir resistance. The U.S. is currently stockpiling antiviral drugs at the federal, state, and local levels and the Department of Health and Human Services (HHS) has published recommendations for the distribution of limited antiviral drug supplies. However, HHS does not prioritize healthcare worker prophylaxis and gives top priority to hospitalized patients with influenza, a group in which the effectiveness of antiviral drugs is unknown. At this time, federal and state antiviral stockpiles are designated for treatment only. During a pandemic, it is likely that many hospitals will be overwhelmed following a large surge in patients and high rates of healthcare worker absenteeism. Of the 13 hospitals that responded, only three (23.1%) indicated that they currently stockpile an antiviral drug for influenza. None of the hospitals maintain sufficient stockpiles based on the number of staff with patient contact. Since it was hard to attain specific data on the number of...
personnel with patient contact who were vaccinated at the hospital it is difficult to draw any strong conclusions regarding personnel vaccination. However, the results are suggestive of low vaccination rates, which underscore the need for sufficient supplies of antivirals.

Conclusions: It is critical that the essential services of hospitals be maintained. The government does not currently prioritize the treatment or prophylaxis of healthcare workers. Hospitals should stockpile antiviral drugs (primarily oseltamivir and also zanamivir) to provide for prophylaxis of healthcare workers with patient contact and treatment of their immediate family. The FLR is grossly unprepared for a pandemic in regards to antiviral stocks.
Reliability of EMS and ED Screenings for Depression and Cognitive Impairment

**Background:** While older adults (age ≥ 60 years) are the fastest growing age group in the US, studies indicate that current services are not adequate to identify those at risk for preventable diseases. Therefore, novel approaches are being tested that use non-traditional resources, such as the emergency medical services (EMS) system and the emergency departments (EDs).

**Objective:** This study evaluated the reliability of an EMS screening program for depression and cognitive impairment during emergency responses.

**Methods:** Older adult patients (N=131) were screened by EMS personnel during emergency responses. The screening survey included the PHQ-2, a depression screening instrument that has been previously validated, and the Six-item Screen (SIS), a screening instrument for cognitive impairment. Once the patient arrived in the ED and consented to be in the study, the patient was re-screened using the PHQ-2 and SIS by trained study personnel. The data were analyzed to determine the percent agreement between the two applications of the instruments and to determine the Spearman correlation coefficient.

**Results:** Of the 131 patients screened by EMS, depression-screening results were available for 122 patients and cognitive impairment screening results were available for 125 patients. The average age was 78 years (age 60-94), and 64% were female and 39% were male. Of the patients screened, 60 (49%) screened positive for depression and 20 (16%) screened positive for cognitive impairment. For the same patients screened in the ED, 51 (42%) screened positive for depression and 18 (14%) screened positive for cognitive impairment. Overall, for the PHQ-2, the EMS results and ED results agreed 73% (95% confidence interval: 64%-81%) of the time. The Spearman correlation was 0.46, indicating moderate correlation. For the Six Item Screen, the EMS results and ED results agreed 88% (95% confidence interval: 81%-93%) of the time. The Spearman correlation was 0.50, indicating moderate correlation.

**Conclusions:** Older adults cared for by EMS have high rates of depression and cognitive impairment, as screened by the PHQ-2 and the Six Item Screen, respectively. EMS-based screening is moderately reliable, as compared to repeat testing in the ED. The validity of these screening results is not known and needs to be further investigated.
Basic Science and Clinical Research

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Time-Motion study of Emergency Pharmacist Activity in an Academic Emergency Department

Objectives: A time motion study was conducted to determine how an emergency pharmacist (EPh) spends his time on emergency department activities. Observations of tasks performed, communication events with other health care providers in the ED, and methods of communication were collected.

Methods: The study was conducted for an 8 week period during summer 2007 in a 120 bed level 1 trauma centre Emergency Department with a patient volume of 100,000 visits per year. IRB approval was obtained. The ED-based Clinical Pharmacist was followed in 4.5 hour blocks of time by two medical student investigators who recorded time spent on various activities and the type of activities performed. The activities were classified as tasks, communications or interventions. Communication events included data on duration, mode, topic, location, direction and interruption. Frequency and duration of events were calculated for each measure. Descriptive statistics were calculated to aid in interpreting the data.

Results: One thousand three hundred and two total events were recorded during a total of 59 hours and 24 minutes. General patient care tasks performed by the EPh accounted for 54.1% of the total events recorded and 77.3% of total time recorded. Communication tasks accounted for 45.2 of total events and 22.4% of total time recorded. Interventions made by the EPh accounted for the remaining 0.7% of total events and 0.3% of total time recorded. Of the tasks performed by the EPh, it was observed that most time was spent on Trauma (24.4% of total time) and roaming, defined as walking throughout the ED for purposes such as checking in with staff and scanning the patient tracking boards (21.3% of total time). Communication was primarily with nurses, residents, and attending physicians, although time spent in communication with and the reasons for the communication varied with each group. The majority of the communication events in all groups were initiated by the person in communication with the EPh. Of the nine intervention events recorded, eight were alternative drug suggestions made by the EPh.

Conclusions: A significant proportion of total activities recorded during the time motion study were directly observed to be related to patient safety. The activities of which the EPh spent the highest percentage of time were communication events, roaming, and resuscitation efforts, all of which can attribute to an increased patient safety function in the emergency department. There were fewer interventions than expected, likely due to the high rate of prospective consultation given to providers and nurses.
Survey of Dermatologists' Attitudes and Practices with Regard to Mental Health Referrals and the Use of Psychotropic Medications in Psychocutaneous Disease

Background and Objective: Until recently, medical specialties have been well defined in the types of patients they see, however, it is becoming clear that many of them overlap with one another as patients present with diseases that merge different specialties. Current literature suggests the need for increased collaboration between psychiatry and other medical specialties including primary care and dermatology. In the fields of psychiatry and dermatology, the overlap is through psychophysioologic disorders, specifically, psychocutaneous diseases. Psychocutaneous diseases are defined as skin disorders like acne, eczema, and psoriasis which are exacerbated by stress. There have been a number of studies that highlight the development of these diseases from a macroscopic and a microscopic perspective with heavy interest in both psoriasis and eczema. These studies clearly link excessive stress with a significant decline in treatment outcomes. Another area of overlap between these two specialties is with primary psychiatric disorder, where patients have a psychiatric problem first and no intrinsic dermatologic disorder. This group includes: delusions of parasitosis, body dysmorphic disorder, trichotillomania, dermatitis artefacta, neurotic excoriations, anxiety, and obsessive-compulsive disorder. Though existing literature suggests that many dermatologists are already prescribing psychiatric drugs, there have been few studies that attempt to follow the practices and attitudes of dermatologists regarding the management of patients with these complex afflictions. This project will attempt to quantify the level of confidence dermatologists have in diagnosing and managing their patients that also have psychiatric illness in the upstate New York communities.

Methods: A cross-sectional study of dermatologists from Upstate New York (including 7 from Detroit, MI) who are members of the American Academy of Dermatology and patients from upstate New York. Forty-five physicians and 83 patients participated in the study. A physician survey was designed to determine dermatologists' practices and attitudes and had two parts totaling 14 questions: the first component focused on practices regarding psychocutaneous diseases and the second component covered primary psychiatric disorders (defined above). The second survey was designed for patients and intended to identify patient stress level, emotional state, and psychological effects that the disease might be having on their lifestyle and activities.
Key Results:

Discussion of Findings and Conclusion: There are important findings worth mentioning regarding the surveys. Twenty-nine percent of dermatologists believe that patients are more willing to accept psychotropic medication from a dermatologist than a psychiatrist. This opinion may impart be due to the social stigma associated with mental illness.

The results show that only 7% of dermatologists believe they received the adequate training necessary for prescribing psychotropic medication. The bar graph above illustrates that a large percentage of dermatologists' patient populations have a psychiatric illness. This suggests that most dermatologists may not have the training required to manage these patients and may need to refer them to a mental health provider. The results show that only about half (49%) of dermatologists are actually referring their patients with psychocutaneous disease. This implies that dermatologists are attempting to treat some patients with psychophysiologic diseases themselves without a referral to mental health professionals. The results also show that roughly one out of every four dermatologists is comfortable prescribing an anti-depressant, while only one out of twenty-two believes they can prescribe antipsychotics. Of note, 29% of dermatologists say they currently offer stress reduction services. How good are dermatologists doing in treating the "entire patient"? The patient survey shows that 71% of them feel they are only receiving treatment for their physical symptoms and would like alternative treatment options including stress reduction services, psychotherapy/counseling, and improving self-esteem to treat the other manifestations of their illness. In subgroups with a strong psychocutaneous linkage, the desire for alternative services beyond physical symptoms was significantly higher in patients with psoriasis (88%), dermatitis/eczema (86%), and acne (100%). Clearly, there is a need to improve the education of dermatologists on management of psychiatric patients that includes a better understanding of psychocutaneous and primary psychiatric disorders or a need to refer more of these patients to psychiatrists or other mental health providers. These types of patients are a significant portion of a dermatologists' case load and therefore warrant a change in practice and better collaboration with mental health professionals to help meet their patient needs and provide continuity of care.
Abstract: The hepatorenal syndrome (HRS) is a syndrome of functional renal failure in the setting of end-stage liver disease (ESLD). There are three factors involved in its pathogenesis: 1) hemodynamic changes that decrease renal perfusion pressure, 2) stimulated renal sympathetic nervous system activity, and 3) increased synthesis of humoral and renal vasoactive mediators. The interplay between these pathways is complex and currently not well understood. The acute form of HRS is rapidly progressive and has a poor prognosis, with 80% mortality at 2 weeks. The only known effective therapy for HRS is orthotopic liver transplantation. Unfortunately, it is estimated that only 35% of those with HRS survive to transplant or discharge. In order to promote subsequent mechanistic studies and interventional trials that will address critical unmet needs, we performed multi-organ gene expression profiling in an attempt to elucidate a common molecular profile in tissues central to the development of HRS. The ultimate goal of this research was to develop a blueprint for crosstalk between disparate organ systems in the pathogenesis of functional renal failure in the cirrhotic patient.

Objectives: Researchers hypothesized that the hemodynamic changes associated with portal hypertension may be a result of change in pressure and shear stress applied to the endothelial surface of mesothelial vasculature. Further, researchers believed that differential expression of cytokines, particularly IL-6 and IL-8 may be responsible mechanistically for those changes. In particular, with regard to splanchnic endothelium, we explored whether an early pattern of signal transduction and cytoskeletal re-organization indicated by a unique mRNA profile was correlated with the hemodynamic alterations and renal manifestations of ESLD.

Methods: Experimentation was carried out using containing human vascular endothelial cells (HUVECs) enclosed in special pressure-sealed chambers which allowed researchers to apply different levels of pressure and shear stress to the cells. Gene products of the cells in both experimental and control cell groups were collected and analyzed for differential expression. Assays were carried out using real-time quantitative PCR assay using a Roche Light cycler and either SYBR-green or TAQman detection and in select instances with the use of nucleic acid based microarrays, immunohistochemical analysis of the site of gene expression, and fluorocytometric bead assay.

Results: Analysis of HUVEC lines showed a differential expression of IL-6 and IL-8 between control and experimental groups.

Conclusions: IL-6 and IL-8 are differentially expressed in HUVECs subjected to increased pressure and shear stress. Further research is required to show if these changes are a causal agent in the hemodynamic changes observed in portal hypertension and hepatorenal syndrome.

References:

Basic Science and Clinical Research

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Endothelial Cell Expression Of IL-6 And IL-8 As A Result Of Pressure And Shear Stress In A Model For Hepatorenal Syndrome
Long QT and Coronary Disease

Objectives: Previous studies of Long QT Syndrome (LQTS) have focused primarily on the clinical course of affected patients within the first four decades of life. This study examined the effects of coronary disease on LQTS patients who were over 40 years old.

Methods: The study population involved 641 patients older than age 40 who had QTc>449ms. Patients were identified as having coronary disease if they had a history of hospitalization for myocardial infarction, coronary angioplasty, coronary artery bypass graft surgery, or were treated with medication for angina. LQTS-related cardiac events included the first occurrence of syncope, aborted cardiac arrest, or sudden cardiac death without evidence suggestive of an acute coronary event. Cox proportional hazards regression modeling was used to analyze the independent contribution of coronary disease to LQTS-related cardiac events.

Results: Time-dependent coronary disease was associated with an increased risk of LQTS-related cardiac events as shown in the Mantel-Byar graph and by Cox analysis (hazard ratio 2.24, 95% confidence interval 1.24-4.04, p=0.008) after adjustment for syncopal history before age 40, QTc, and gender. Factors such as diabetes and hypertension that increase the risk for coronary disease were not associated with an increased risk for LQTS-related cardiac events.

Conclusions: This is the first study to demonstrate that coronary disease augments the risk for LQTS-related cardiac events in LQTS. The findings highlight the need for more focused preventive therapy in LQTS patients above the age of 40.

References:
Long QT Syndrome: Increased Risk of LQTS-related Cardiac Events with β-agonist Therapy for Asthma

Objectives: The aims of this study were to determine the risks involved with inhaled β-agonist bronchodilators for asthma in patients with the inherited long QT syndrome (LQTS) and to evaluate the effects of P-blocker therapy on outcome in LQTS patients with asthma.

Background: The clinical course and risk factors associated with β-agonist therapy for asthma has not been previously investigated in the LQTS population.

Methods: The risk of a first LQTS-related cardiac event due to β-agonist therapy was examined in 3,287 patients enrolled in the International LQTS Registry with QTc≥450msec. The Cox proportional hazards model was used to assess the independent contribution of clinical factors for first cardiac events (syncope, aborted cardiac arrest, or sudden death) from birth through age 40.

Results: Time-dependent β-agonist therapy for asthma was associated with an increased risk for cardiac events (hazard ratio [HR] = 2.00, 95% confidence interval 1.26- 3.15, p = 0.003) after adjustment for relevant covariates including time-dependent P-blocker use, sex, QTc, and history of asthma. This risk was augmented within the first year after the initiation of P-agonist therapy (HR = 3.53; p = 0.006). The combined use of P-agonist and anti-inflammatory steroids was associated with an elevated risk for cardiac events (HR= 3.66; p < 0.01). P- blocker therapy was associated with a considerable reduction in cardiac events in those using P-agonists (HR= 0.14; P = 0.05).

Conclusion: β-agonist therapy was associated with an increased risk for cardiac events in asthmatic patients with LQTS, and this risk was diminished in patients receiving P-blockers.

References

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Cognitive Function in Children with Sickle Cell Disease

Objectives: Cerebrovascular damage and associated neurocognitive delays begin early in sickle cell disease (SCD). Given the pathophysiology of SCD, we hypothesized that measures of hemostasis (platelet count, soluble CD40 ligand (sCD40L)), inflammation (C-reactive protein (CRP), sCD40L, white cell count (WBC)), hemolysis (hemoglobin (Hb), lactic dehydrogenase (LOH)), and/or oxygen saturation, would be associated with poorer performance on a battery of neurocognitive tests in children with SCD. Our primary aim is to acquire preliminary data regarding the above associations and to assess the mediating roles of tested variables. Secondary objectives include the examination of relationships between the evaluations noted above and (a) behavior assessments and school performance; (b) cerebral transcranial Doppler (TCD) ultrasound velocity; (c) history of neurological symptoms and (d) other significant clinical complications (pain crises, acute chest crisis, proteinuria) in this population. The data provided by this investigation should inform future studies regarding early risk stratification and the pathophysiology underlying particular neuropsychological delays.

Methods: A cross-sectional, within group design is being used. It is anticipated that 60 subjects, ages 2.6 to 16.99 years old with a diagnosis of Hb SS, SC, S thal, or Hb SD will participate. At the first study visit systemic oxygen saturation (Sp02) and cerebral oxygen saturation (rS02) are monitored, a physical exam is performed, pertinent medical history is obtained, and laboratory studies are procured. At the second visit neuropsychological tests are administered. These include: Weschler Tests of Intelligence (WPPSI-III or WISC-IV), Connor's Continuous Performance Test-II (CPT-III-K-CPT), NEPSY: A Developmental Neuropsychological Assessment, and Woodcock Johnson Tests of Achievement (WJ-III ACH). A Behavior Rating Inventory of Executive Function (BRIEF) is filled out by the parent/guardian. Teachers assess intellectual ability, attention/executive function, and achievement after the second visit is completed. Descriptive statistics and Pearson correlation coefficients were obtained for some preliminary data and significance (2-tailed) was tested.

Results: To date 12 subjects have been enrolled in the study and have completed the first visit. Five subjects have completed neurocognitive testing. Characteristics of this population: 9 males, 3 females; median age 8 yrs. 7 mos. (range 2yrs. 11mos. to 15yrs. 9mos.); genotype- 5 Hb SS, 3 SC, 3 S thal, 1 SD. Pain episodes/yr= 0 in 6 subjects, 5 in 4, >5 in 2. No subject has a history of stroke, transient ischemic attack or spleen sequestration and all have normal neurological examinations. One subject has a history of priapism. Three have known learning disabilities. Four subjects have taken the WJ-III ACH and displayed the following range of standard scores: Broad Reading 89-106, Broad Math 64-105 (normative mean=100, SD=15). Four BRIEF Parent Forms were completed. The BRIEF Parent Form Global Executive Composite (GEC) T-scores range from 36 to 65 (mean=50, 60-64=mildly elevated). Statistical relationships between studies and cognitive tests cannot yet be performed given the small number of subjects who have completed testing. Correlations between other studies obtained to date were examined.
Hemostatic markers: There were no study correlations with platelet count. sCD40L assays have not yet been run and could not be tested. Inflammatory markers: CRP was correlated with WBC \( (r = .857; p = .045) \) and lactate levels \( (r = .893; p = .001) \). In addition to its relationship to CRP, WBC was negatively correlated with Sp02 \( (r = -.639, p = .025) \) but not with rS02. Hemolytic markers: Hb was correlated with LDH \( (r = -.668; p = .025) \), Sp02 \( (r = .863; p = .001) \), rS02 \( (r = .749; p = .005) \) and TCD velocity in both middle cerebral arteries (MCAs) \( (RMCA: r = -.743; p = .035; LMCA: r = -.763; p = .027) \) and in the left internal carotid artery (dICA) \( (r = -.773, p = .025) \). Oxygen saturations: Sp02 was correlated with WBC, Hb, and TCD velocity in both MCAs as noted. RS02 was correlated with Hb, and TCD velocity in both MCAs as noted.

Conclusions: Study procedures are fully feasible as evidenced by the ability to enroll and test 12 children with SCD over 3 months time. To date, many correlations noted in this study corroborate correlations found in investigations of larger populations. Notably, cerebral oxygenation has not been well studied in children with SCD and negative correlations with TCD velocities in the MCAs are intriguing. Larger subject numbers will be needed to test the primary hypothesis of this investigation.
An Individualized Approach to Breaking Bad News

Abstract:
One of the responsibilities of a physician is being in the unfortunate position of having to communicate bad news to patients. Doctors are repeatedly faced with the task of delivering unwanted and sometimes unexpected information to their patients. The severity of this news can range from diagnosing the common cold or assessing the need for routine immunizations to diagnosing cancer and other life-threatening or terminal illnesses or informing patients that treatment options can no longer be expected to have a curative effect. It can be expected that any time an individual receives bad news, he will, to some degree, perceive the experience as negative and will undergo a host of psychological responses. However, as healthcare providers, it is our duty to explore ways in which we can minimize the pain and suffering that our patients feel when receiving bad news.

Receiving bad news has been linked to feelings of anger, fear, anxiety, helplessness, hopelessness, shame, relief and guilt (1). The range of emotions experienced varies among individuals (2). It is typically the approach of the person bearing the bad news to attempt to minimize negative affects and choose an approach that will facilitate patient satisfaction, quality of life and well-being (3). A patient-centered approach to delivering bad news has been associated with more positive variables such as perceived hope, appropriateness of the information given, physician availability and emotionality, physician non-dominance, satisfaction, and less anger and depression (3). Although emotional pain may be a necessary step in allowing the patient to adapt to the news he has just received, there are ways in which negative responses can be reduced (1). We would like to suggest that the patient-centered approach to breaking bad news be extended to include a conversation in which the individualized preferences of each patient are elicited in order to gauge how the individual would like to receive bad news, while of course making it known that the patient is free to change his mind at any time.

Individualized care is characterized by altering how much and how soon information is conveyed to the patient in order to account for the patient's needs, allowing for a supportive relationship to be formed between the patient and physician (4). Girgis and Sanson-Fisher suggested that individualized disclosure, in which the physician assesses how and when to deliver information to the patient, is preferable to both non-disclosure and full disclosure (4). However, because the emotional response to bad news and preferences for how bad news is delivered differ from person to person, a physician's expectation for how a patient will respond to bad news is likely to be incorrect (5). If a physician decides to withhold information, assuming that the patient would not like to hear it at the given time, the patient may feel that he has not received adequate information and may experience unnecessary anxiety (6). Fulfilling a patient's wishes of knowing desired details about one's illness may have therapeutic effects and may prevent the avoidable emotional stress associated with uncertainty of one's health status (7). Individualized care may allow the physician to be perceived by the patient as partnership-oriented, a style that facilitates patient satisfaction and lowers anxiety and depression subsequently experienced by a patient who has received bad news (3). Therefore, when possible,
individual preferences should be determined prior to the point when a physician would have to assess
the situation without a patient's direct input.

Allowing patients to state beforehand the way in which they would like to hear bad news has been
shown to yield lower levels of anxiety and a higher overall satisfaction level with the experience of
receiving bad news (8). Satisfaction level is important, not just for the patient-physician relationship, but
also in determining treatment compliance and adjustment to and acceptance of the information
provided (5). Certain preferences that vary among individuals, like who is present at the time of
diagnosis, directly impact patient affect. Having those preferred individuals present at the time of
diagnosis has been associated with lower patient anxiety. Similarly, individualizing the amount of
information provided regarding life expectancy has also been linked to lower levels of anxiety (8). In
addition, this type of approach would allow the patient to display his own autonomy by involving him
in the process, allowing him to have a sense of control over his illness. Baile, et al have termed this the
patient-focused beneficence approach to breaking bad news (9).

Given this compelling data, we would encourage physicians to take the time to have a discussion with
their patients in order to elicit individualized preferences for how information is conveyed. By
including this discussion when informing patients of all the possible outcomes for a symptom or
clinical finding, some of the negative affects associated with receiving bad news may be minimized.
For example, if a woman presents for a fine needle aspiration of a breast lump, a discussion should
ensue prior to having the procedure in which she is informed of all possible outcomes and asked
specific questions in order to determine her preferences for receiving bad news. The patient should be
given the opportunity at this time to state if and how much information she would like when initially
informed of her diagnosis (including actual diagnosis, prognosis and treatment options), if she wishes
to hear this information as soon as it is learned, if she wishes only to be called into the office to hear
the information or if she would prefer to receive the information over the telephone, who if anyone she
would like to be present when the information is given aside from the healthcare provider delivering
the news, if she wishes to hear the news in purely medical terms or if she prefers that the physician use
language devoid of medical jargon, if she wishes to receive written information about diagnosis and/or
treatment options, if she wishes to hear cases of others in similar situations, preferences for personal
contact, if she wishes to hear how this diagnosis is likely to impact other aspects of her life, etc.
Knowing these preferences in advance will enable the physician to be better prepared for the session,
to come with any additional information the patient had previously requested and to be prepared to
answer certain questions. In addition, fulfilling a patient's wishes is likely to result in a higher rating of
patient satisfaction with physician-patient communication (8).

Engaging in dialogue that focuses on patient preferences will also open the conversation to possible
outcomes of a patient's symptoms or clinical findings. A detailed discussion of expected or potential
outcomes will prepare the patient for the bad news and reduce shock associated with final disclosure, a
situation that has been shown to be coupled with lower levels of anxiety (8). In addition, this will open
the door for better communication, thus it is likely to reduce the feelings of mistrust, anger, fear and
blame that are often associated with poor communication (10).

Including a discussion of this nature any time there is the potential for bad news to be delivered may
prove to be time-consuming. However, physicians themselves experience stress and anxiety when
faced with the task of delivering bad news. Strong patient emotions can lead the physician to
experience feelings of anxiety, guilt or failure (11). Delivering news of any nature, bad or good,
produces a stress response, characterized by cardiovascular responses and self-reported distress. Bad
news delivery, however, results in more marked changes in cardiovascular, psychological and natural
killer cell functions, all characteristic of an acute stress response (12). A survey of oncology fellows
found that breaking bad news was repeatedly mentioned as a major stressor. Certain issues surrounding
the topic, particularly initiating the dialogue, was noted to be especially difficult (13). It is possible that the physician's stress and anxiety can also be reduced if patient preferences were determined prior to the time of information delivery. Having a detailed conversation earlier regarding patient preferences can set the stage for the bad news conversation to follow. While we do not suggest that breaking bad news will then be easy, it is possible that the task may be perceived as less stressful if the subject had been discussed previously. Easing patient anxiety results in greater physician satisfaction (14). By ensuring that they had taken the steps to minimize patient anxiety and increase patient satisfaction by presenting information in the way the patient wishes to hear it, doctors may experience less of an acute stress response when confronted with the task of breaking bad news.

We would like to acknowledge that there are many instances in which having a discussion of patient preferences regarding specific details of how bad news is given may not be possible. However, physicians need to first elicit patient preferences in order to actualize them (15). We hope that this information will prove useful to clinicians and will encourage them to embrace the opportunity to elicit individual preferences for how bad news is disclosed whenever possible.

References
Community Health Research

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Project FIRM (Family Insulin Resistance Management)

Abstract:
Childhood obesity is a major problem facing the United States. This condition is associated with a number of comorbidities including cardiovascular, endocrine, and psychosocial consequences. Many of the comorbidities that would otherwise not present until late adulthood are beginning to affect children at younger and younger ages. This causes increased emotion, physical, and financial stress on the family and overburdens an already taxed health care system. The risk factors for childhood obesity stem from lifestyle, family, and societal causes. To help combat those individual factors (lifestyle and family issues) Project FIRM (Family-based Insulin Resistance Management Study) began in March 2005. Project F.I.R.M.'s aim is to treat obesity in children, via the family's attitudes and practices. By addressing and hopefully changing an entire family's lifestyle, we believe we can begin to eliminate some of the environmental causative factors of childhood obesity. The study is designed to provide interventions through a series of five weekly to biweekly hourly appointments to underserved families with obese children in the Rochester area. The interventions are meant to qualitatively assess family dynamics and attitudes towards food, nutrition, and lifestyle, and hopefully decrease the child’s body mass index, which is measured at each intervention session. In the summer of 2007, one year follow-ups will be conducted with those families who finished the series of interventions the previous year, and new families will be enrolled in Project F.I.R.M. While these new families undergo the same series of five interventions, quantitative assessment of the child's BMI, and qualitative assessment of family dynamics will be made. Four families were enrolled the summer of 2007 with 2-4 visits completed for each family. Although improvements were made in enthusiasm and knowledge, no changes in BMI were seen in any child enrolled in the study.

Objectives: To improve the health, nutrition, and exercise habits of low-income families with overweight or at risk for being overweight children

Methods: Five hourly sessions with the family and an investigator to discuss how to incorporate better nutrition and exercise into their daily lives.

Results: Four families were enrolled the summer of 2007 with 2-4 visits completed for each family. Although improvements were made in enthusiasm and knowledge, no changes in BMI were seen in any child enrolled in the study.

Conclusions: Project FIRM is not successful in changing the BMI of children enrolled in the study. Limitations of this study include the short time period, the small amount of hours, and lack of better and more diverse measurement values such as change in body fat or change in total caloric intake.

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Community Health Research

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**UR Well Student Outreach at St. Joseph's Neighborhood Center**

**Background**
St. Joseph's Neighborhood Center provides the uninsured with appointment-based healthcare and counseling services on a sliding scale. Most healthcare visits cost $5. For new patients and for complete physical examinations the fee is $15. As articulated on St. Joseph's website, [http://www.sjncenter.org/](http://www.sjncenter.org/) "services will never be denied to an inability to pay". Any required laboratory work, e.g. fasting lipid profile, is passed on to the patient at the cost ACM laboratory charges SJNC. SJNC is open from 9-5 Monday-Thursday and 9-4 on Friday. By partnering with SJNC, the UR Well clinic is able to operate out of SJNC providing primary care services to the uninsured on Tuesday nights from 6-9 pm. This allows many patients who work during the day to receive healthcare with less worry of interfering with work. This is particularly important as approximately 59% of our patient population is employed. Each Tuesday evening we have 1 administrative coordinator, 2 front desk students, 1 medical assistant, 3 healthcare teams, and a primary care physician preceptor. Each healthcare team consists of a health team junior, 2nd year student, and a health team senior, a 3rd or 4th year student who has completed the medicine block during the clinical years. Recently we have been able to expand our services to include neurology on many Tuesday nights. Neurology now has its own healthcare team and operates similarly to the primary care branch of UR Well.

**Who We Serve**
In the first three years of operation, the UR Well Student Outreach Project provided care for approximately 282 patients. This year alone we have provided care for 74 patients from June 2006 to May 2007. Demographic data were extracted from surveys administered to patients at their first visit. 58% were male and most were non-white (57%), including 45% African American, 29% Hispanic, 9% Other and 2% Asian. Most are employed (59%), although 79% earned less than $20,000 in the previous year. Only 22% had a college education. The average age was 37 years, ranging from 16 to 83.

**Future of UR Well**
Starting in October 2007, UR Well will be partnering with Strong Vision, Project Eye Care, and the Ophthalmology Department to open a monthly ophthalmology clinic at SJNC. The clinic will see about 6 patients per night with a dedicated student team trained by a resident or attending. The ophthalmology interest group will also be helping out. Also in the same month, UR Well will be expanding its services to the homeless of Rochester. Collaborating with Unity Homeless Project, Department of Family Medicine, and Monroe Department of Public Health, we will be offering quarterly mass TB screenings, monthly immunization outreach, and on-going screening projects at homeless shelters. Later on in the fall, we plan on developing group health education curricula for the patients at SJNC and/or the homeless shelters. The groups will be based on four themes, such as diabetes, women's health, general wellness, and mental health, and each group will be held once a month.
Strong Stories

*Strong Stories* is a television show that brings together students at the University of Rochester School of Medicine and WXXI, the Rochester PBS affiliate, to tell real patient stories in order to spread community awareness about public health concerns. Prior to this project, a pilot episode had been produced, but the framework for the show’s organization and structure was not in place.

In order to facilitate the production of this TV show, a series of tasks were undertaken to create an infrastructure for both the student responsibilities and the episode subject matter.

Student roles for production were established, as were the operational procedures for each episode. A flow chart of the production of an episode was created. In addition, an educational program and packet were created to assist students through the process of conceptualizing a television episode, creating a story, interviewing skills, and writing a script.

Subsequently, a list of potential episode topics was generated, and physicians were contacted in to determine if they could suggest a patient to be profiled in an episode, and their willingness to participate on camera as the treating doctor. Approximately 50 such health care providers were identified.

With this infrastructure development, *Strong Stories* is ready to commence producing, and is confident that all of the foundational needs of show are in place.
Barriers to HIV/AIDS vaccine trial enrollment in Soweto, South Africa: a qualitative approach

Abstract
Each day 14,000 men, women and children are infected with HIV worldwide. Sub-Saharan Africa has been the most severely impacted by the disease, with the highest number of HIV positive individuals in the world (29.4 million people living with HIV/AIDS). International collaboration to develop a preventive vaccine has taken the form of the HIV Vaccine Trials Network (HVTN), which provides international cooperation for designing, conducting and analyzing Phase I to III clinical trials of HIV vaccines. The HVTN 503 ("Phambili") trial in South Africa addresses the critical question of the role of clades (subtypes) in vaccine protection. The study also evaluates the efficacy of this vaccine in reducing the proportion of participants who acquire HIV infection, or decreasing the HIV viral load set point upon infection. Students worked as clinical trial specialists under the Phambili study to observe reasons for enrollment and barriers to continuity of participation. The aim of this qualitative research was to understand what barriers are most prevalent in HIV education and prevention in Soweto.

The researchers observed and documented community reactions during all aspects of the trial protocol, from recruitment in the local community, to pre- and post-test counseling and participant enrollment in the clinic. Resistance to knowing one's HIV status was the most frequently encountered barrier. Other major challenges to trial enrollment included: negative attitudes about research and research institutions, lack of understanding of vaccines, and confusion about research methods. Women also faced unique challenges due to the requirements of the trial, mainly family planning.

The main barriers to enrollment are reflective of the strong stigma associated with HIV in South Africa and the associated psychosocial repercussions. The challenges to HIV prevention are multi-dimensional and often intertwined- stress, ostracism, and physical violence were often cited reasons for denying participation in the trial. The role of women in society and their lack of power in relationships are also reflective of this stigmatization. Strategies for trial enrollment should revolve around HIV prevention and establishing baseline education about HIV and STDs to supplement vaccine trial initiatives. There is a general need for a unified system of education about general basic health awareness and HIV transmission and prevention so that information is consistent, correct, and de-stigmatized. Increased collaboration among grassroots, government, and local community groups is an integral step towards effective HIV prevention.
Abstract:
End-of-life care is a much-needed service in South Africa, and an important emerging field of research worldwide. Of the approximately 56 million deaths in the world every year, nearly 85% occur in the developing world. The WHO has recently recognized the urgent need for minimum standards of pain relief and palliative care, as well as initiation and development of palliative care programs suitable for communities’ cultural, social, and epidemiological circumstances. The Hospice Association of South Africa was founded in 1986, and currently there are about fifty hospice organizations, mostly non-governmental organizations, serving populations around the country. However, like many health services in South Africa, these organizations are distributed unevenly, and there are no formal end-of-life services in the Limpopo Province. Little has been published about the people using the existing services, or people's desire to extend palliative and hospice care to underserved areas.

The aim of this project is to generate a narrative description of the circumstances in which terminally ill people are cared for by collecting primary data through direct observation and interviews in the city of Acornhoek, South Africa.

Objectives: The objective of this research is to get a preliminary understanding of care provided near the end of life in Acornhoek, South Africa by interviewing a number of healthcare providers, family caregivers, patients, and community members about these perspectives using a semi-structured interview technique.

Methods: In terms of participant selection, the goal is to include in the study health care providers, patients and family members, as well as adult members of the community served by Tinstwalo Hospital. Sampling will aim to cover a range of perspectives on the nature and quality of care at the end of life, allowing for comparison between different perspectives. Data will be generated using field observation, as well as a series of approximately 8 semi-structured, in-depth, individual interviews.

Results: Eight (8) interviews were conducted. Participants included staff physicians, medical students, IDV/AIDS counselors, Sister Nurses (nurse practitioners), a traditional healer, and residents of Acornhoek and the surrounding villages. One longitudinal case study was performed.

Conclusions: Initial analysis of the results indicate that care for the terminally ill in this rural South African community is characterized by a mosaic of traditional practices, family support, modern...
medical interventions, and home-based (or "village-based") care. However, options for care at the end of life in Acomhoek are severely constricted by widespread poverty and inequality of access to basic services, such as adequate housing, transportation, nutrition, clean water, and medical care. HIV/AIDS is a major contributor to morbidity and mortality, and its social and epidemiological burdens are felt acutely near the end of life.

References
Modeling Healthcare Perspectives from Six European Countries

Abstract:
In this international narrative research study, I used facets of European healthcare systems, as told by patients, to model fresh healthcare perspectives for an American audience. I highlighted the Netherlands, Latvia, Germany, Italy, Ireland and Spain. By yoking my passion for writing to a healthcare related human interest piece, I hoped to maximize my experience in Narrative Medicine.

Objectives:
- To compose creative non-fiction narratives about healthcare issues.
- To describe perceptions of physical and mental hygiene, with special focus on preventative habits.
- To explore perspectives regarding access to and quality of healthcare, barriers to care, and attitudes toward the patient-doctor relationship.
- To research health care policy for each study country, and to integrate this information into the written accounts.

Methods:
The project proposal received RSRB approval for exemption. Local contacts aided in my finding one to two English-speaking subjects to interview in each country. The content and course of the interview was largely under the control of the subject, led by open-ended prompting by myself. English fluency introduced significant selection bias, but I did not intend my project outcome to be a balanced sampling of European healthcare. Rather, I meant to gather a flavor of what was occurring in non-American healthcare, to encourage open-mindedness and thoughtful reasoning about healthcare systems in the public here at home. Once home, I added an additional narrative from an American subject using the same strategy employed in Europe.

Results:
Interviewed subjects were impressively thoughtful in their responses. The personality of each interview varied greatly. Some commanded a clear knowledge of their country's healthcare system; others displayed an almost passive ambivalence. I have conducted ten interviews in Europe, and produced ten narratives of my own style.
**Conclusions:**
Interestingly, many of the current Presidential candidate's proposed platforms for expansion of health care in the United States have an essence of the systems I encountered during my travels. Some exemplary discussion of the candidate's ideas could be a prudent future direction to my project.

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International Medicine Research

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A Study Examining Antenatal and Postnatal Care in a Malawian Village: Follow-up and Reassessment of Knowledge Base and Health Outcomes

Background: The Gowa Health Promotion Project was initiated in 2005 to assess the needs of Gowa, a small village in Malawi, Africa. The study determined that there is a crucial need for improved teaching methods and sources of information for antenatal care classes. The current study aims to continue the project by reexamining the antenatal health curriculum developed in 2006 and determining how it can be made effective for self-sustenance and dissemination. Reassessment of antenatal and perinatal knowledge, resources, and practices will be useful in evaluating the progress of the project, and will contribute to improving services and teaching methods in Gowa.

Objectives: 1. Assess the use and effectiveness of the antenatal health curriculum instituted in 2006 by evaluating participation, demographic trends, ways to improve participation, and implementing any curriculum modifications. 2. Assess the baseline knowledge of participants and potential participants for antenatal and perinatal health by interviewing women in surrounding communities. 3. Assess the knowledge of clinic staff members, Health Surveillance Assistants (HSAs) and local Traditional Birth Attendants (TBAs) for antenatal care, practices and guidelines. 4. Long term objectives: Tracking clinical data to assess trends in age of gestation when first attending classes and stage of labor when presenting to the clinic, dissemination of a curriculum to surrounding villages, increasing resources availability to health care providers and community members, and continuing to build a long-term relationship between URSMD and the Gowa Health Center (GHC).

Methods: The PIs attended the antenatal care classes lead by Gowa's HSAs to assess their quality and content. HSAs were interviewed to assess curriculum content and effectiveness. 75 women, at least 18 y.o., were interviewed with the use of an interpreter to assess which antenatal and perinatal care practices are currently understood, available, utilized and desired. Knowledge baseline assessment interviews were conducted in several surrounding villages. Interviews were conducted with health professionals involved in labor and delivery to assess current practices, resources available, and desired resources. Data was collected from the GHC registries to monitor maternity clinic attendees and antenatal care class participants.

Results: Interviews with the HSAs, clinic staff and local TBAs revealed antenatal and prenatal knowledge in accord with current guidelines. HSAs stated that the curriculum was being extensively used and additional educational material was provided. The majority of the women surveyed were married, did not work outside of the home, did not have secondary education and denied alcohol, drug and tobacco use. Antenatal class surveys revealed that women enjoyed the classes and the topics presented. Most have knowledge about proper nutrition, self-care prior to labor and delivery and child care. A majority receive pregnancy advice from health care workers and a minority from family
members and village elders. Most prefer to deliver in a supervised setting. Baseline information surveys revealed that most women had received tetanus immunizations and often had polio and measles vaccines. All have/plan to breastfeed for the recommended 2 year duration. Most have had malaria and were treated with antibiotics. Prenatal care regimens consisted of iron, folate, iodine, and antibiotic malaria prophylaxis, SP provided by the local clinic. A review of clinic data reveals most women do not begin antenatal care until late in the second trimester. From July 2006-June 2007, the average age of admitted women was 24.9 years at 38.1 weeks gestation and an average gravida of 3.4. From June 2005-June 2007, there was an average of 24.9 admissions per month to the GHC Maternity Ward, averaging 2.28 days per admission. 92% were spontaneous vaginal deliveries, 7% were referred to the government hospital and 2.7% were stillborn. 7.7% of babies weighed less than 2500 grams.

**Conclusions:** Interviews consistently revealed that financial resources are a large concern in the population and often dictates where/when women seek care, if at all. Additionally, distance to the GHC was a factor in the decision to seek care. Health care providers stressed the need for medications, supplies and additional educational resources. Despite the many limitations faced, the GHC is adequately prepared to handle a variety of birthing situations and readily refers patients to larger hospitals when necessary. Family planning, antenatal services and child health care/immunizations are widely utilized by community members. One area of identified need surrounds the desire to involve the men in family planning and antenatal classes.
Objectives: Italy has a history of economic and social inequalities between its northern and southern regions. The incidence of poverty among southern families (22.4%) is four times that of northern families (5.0%). If southern Italy were its own country, it would have the highest risk of poverty in the EU. In terms of health, the South has a neonatal mortality rate four times greater than the North (5.7 versus 1.3 per 1,000 live births). Recent literature suggests that geographic differences in perinatal healthcare organization and socio-sanitary conditions may explain the disparities in neonatal mortality. This study describes the experience of these conditions and their implications for neonatal health from a mother's perspective.

Methods: Semi-structured interviews and focus groups were conducted with both prepartum and postpartum first time mothers from three sites: Naples and Messina in the South, and Trieste in the North. Interview guides were adapted from the WHO's World Health Survey Instrument, focusing on communication, environment, support, autonomy, and choice of healthcare provider. Notes from the interviews were analyzed for thematic content. A total of 72 women participated in the study (15 in Naples, 31 in Messina, 26 in Trieste).

Results: A model of ideal neonatal care emerged based on three fundamental components: desire for vaginal birth, tranquility during birth, and emphasis on immediate breastfeeding.

Conclusions: Based upon women's descriptions, unnecessary medical interventions, such as elective cesarean sections, interfere with all three aspects of this model. This conclusion underscores the growing concern over differing cesarean section rates between the North (27.4%) and the South (45.4%).

References
Abstract:
The introduction of prevention and condom promotion programs, such as the 100% Condom Use Program, has been successful in producing significant changes in sexual behavior and a decrease in prevalence of HIV among high-risk populations in Cambodia. A study of sex worker sexual behavior from 1997 to 2003 suggested that condom use increased dramatically (Gorbach et al., 2006). In addition, a survey of young adult Cambodian men showed an increase in the use of condoms, especially among those more positive and informed about condoms (Douthwaite & Saroun, 2006). However, there is little information about the sexual behavior of Cambodian women who are not sex workers and whether or not the current educational programs, including the condom promotion program, are effective at influencing their behavior. We believe this is an area of crucial interest because several studies have indicated that sex workers and their clients are a bridge of transmission of HIV and other sexually transmitted infections (STIs) to the general population. These studies suggest the need for condom promotion programs that effectively target non-sex worker intercourse.

Cambodia has the highest national prevalence of HIV in the adult population in Asia and has been combating the AIDS epidemic since the first case of HIV was recognized in 1991. National HIV/AIDS and STI strategic plans have emphasized prevention measures such as health education, condom promotion, and surveillance. In 1998, Cambodia implemented the 100% Condom Use Program (100% CUP), modeled after Thailand's successful program which requires the use of condoms for all types of commercial sex. The 100% CUP also includes safe-sex education for sex workers and their clients as well as a readily available supply of condoms. (Saphonn et al., 2004)

Results of the 2002 HIV Sentinel Surveillance (HSS) showed that the prevalence of HIV is still highest in direct female sex workers (DFSWs) and in indirect female sex workers (IDFSWs), at 28.8% and 14.8%, respectively. Nevertheless there is a downward trend in HIV prevalence in each of these groups along with a concurrent upward trend in the number of DFSWs and IDFSWs (i.e., women who engage in sex work on an ad-hoc basis or as secondary employment) who report consistent use of condoms (Saphonn et al., 2004). A study of sex worker sexual behavior from 1997 to 2003 showed that condom usage increased from 53% to 96% among DFSWs and from 30% to 84% among IDFSWs (Gorbach et al., 2006).

Moreover, the HSS showed a decrease in HIV prevalence and an increase in the use of condoms among male surveillance groups, as well as a downward trend of buying commercial sex services (Saphonn et al., 2004). A separate cross-sectional survey of Cambodian men between the ages of 15 and 24 also showed an increase in their use of condoms and noted that men inside the education system and those who were
more informed about condoms were more likely to use condoms (Douthwaite & Saroun, 2006).

Despite the fact that in 2002 the Joint United Nations Program on HIV/AIDS recognized that Cambodia's epidemic was stabilizing, many Cambodians continue to become infected by HIV and the epidemic is spreading beyond commercial sex workers to the general population. Several studies have reported high rates of unprotected sex among sex workers and their non-paying partners and among sex worker clients and their non-sex worker partners. In one study, even though clients had high levels of HIV knowledge, "almost 40% of those interviewed had sex with women other than sex workers (wives, girlfriends, etc.), but rarely used condoms" (Hor et al., 2005). Likewise, DFSWs reported using condoms only 20% of the time with their non-paying partners, with the most common reason being that they loved them (Wong et al., 2003).

The majority of the studies conducted on sexual behavior focused on high-risk populations, such as commercial sex workers and their clients. Therefore, there is little information about the sexual behavior of non-sex worker Cambodian women and whether or not condom promotion would be as effective at reducing transmission in vulnerable populations such as wives and girlfriends. Such research is crucial to implementing effective HIV prevention efforts.

Objectives:
Our primary aim was to estimate the prevalence of condom use of non-sex worker Cambodian women, aged 18-35. Our secondary aims were to identify their awareness of safe sex and HIV, and to identify reasons why they do or do not use condoms.

Methods:
We recruited subjects from the cities of Phnom Penh, Siem Reap, Battambang, Sihanoukville, and Kratie, Cambodia. We obtained a convenience sample of subjects approached in a variety of sites in these cities (e.g. park, marketplace, etc.). Inclusion criteria stated that subjects must be female, Cambodian, non-sex worker and had never exchanged sex for money, 18-35 years old, and literate (able to read and respond to survey in Khmer). Exclusion criteria included subjects who were male, not Cambodian, had ever exchanged sex for money, less than 18 years old or older than 35 years, or illiterate. Subjects completed a 28-question survey in Khmer about their socioeconomic status, sexual behavior, use of and attitudes toward condoms, and awareness of condom education programs. A cover letter translated into Khmer stating the purpose of the survey with instructions on completing and returning the survey was attached. The survey was anonymous and subjects were not in any way connected to their responses in order to protect their privacy.

Results:
36 women responded to the survey, and 30 participants met the inclusion criteria. Of the six participants who were excluded from data analysis, four were under age 18 and two did not answer how old they were.

The mean age of subjects (n=30) was 23.2 years (SD=3.48). 73.3% of subjects were single and 20% were married. 13.3% of subjects had one or more children. 76.7% held a job and 20% did not work. 73.3% reported living in an urban environment, while 23.3% lived in a rural location. 33.3% reported knowing no English, 3.3% reported knowing "basic" English, and 60% reported knowing "conversational" English. The average number of people living in the subjects' household (including the subject) was 5.97 (SD=2.51).

Because 21 out of 30 subjects who met inclusion criteria reported that they had never had sexual intercourse, we were unable to meet our primary aim, which was to estimate the prevalence of condom
use among non-sex worker Cambodian women, aged 18-35. Of the six women who reported having ever had sexual intercourse, the average age at first experience was 20.83 years (SD=2.56). All were currently married. Exactly half of these women used a condom for their very first sexual intercourse. Interestingly, 83.3% used a condom during their most recent intercourse, even though 66.7% stated that "faithfulness" was their preferred method of preventing STDs.

We were however, successful at our secondary aims, which included identifying subjects' awareness of safe sex and HIV, identifying their attitudes toward condom use, and investigating the amount and sources of sex education they had received. 100% of subjects who responded to the question (n=29) "Do you know that condoms can help prevent transmission of sexually transmitted diseases?" answered yes. When asked where subjects receive most of their information about sex, the majority answered either "magazines/newspapers" or "TV/movies." 56.7% wrote that they knew someone with either HIV or AIDS. 90% of participants felt "very positive" about condoms. When asked about possible reasons why they would not use a condom during sex, 9of20 respondents (45%) answered that they would always use a condom. Of the remaining respondents, the most common reasons given were "loss of intimacy," "uncomfortable," or "do not want to."

**Conclusions:**
Due to our small sample size, we cannot make any broad generalizations about our results. There were some obstacles in recruiting more subjects. Although the survey was translated into Khmer, literacy is still a problem, and many women who were approached were unable to understand the cover letter and survey, even though the majority were very receptive to the investigators and wanted to participate. However, the data do show some interesting trends which could be investigated further in a future study. For example, subjects got much of their information about sex from popular culture and media - this implies that such outlets could be used as the best forums for educational purposes. The Cambodian women who participated in our survey were very knowledgeable about the risks associated with unprotected sex, as well as means of proper protection. Given the still conservative nature of Cambodian society, most unmarried, non-sex worker women do not appear to be having sex. Therefore, any future study should target married women in order to fully explore this topic. We found it especially interesting that the majority of surveyed married women were most recently using condoms with their husbands, even though the majority cite "faithfulness" as their preferred method of preventing STDs. Given that published studies have shown that male clients of sex workers are also having sex with wives/girlfriends, our results may imply that married Cambodian women are aware that faithfulness may not be a practical option.

**References**
What More Can a Person Do?
On the Success and Failure of Community-Based and Individual-Based Interventions in Malaria Prevention

Abstract: Malaria kills 20% of African children; a child will average 1.6 to 5.4 episodes of malaria fever each year. There is no definitive conclusion on the comparative cost-effectiveness of indoor residual spraying (IRS) versus insecticide treated nets (ITNs) in controlling malaria. Estimates for the reductions in infant mortality through IRS use have been reported to range between 41-59%. The effectiveness of ITNs in reducing infant mortality has been reported to be 42%. The available evidence to inform public health policy is severely limited by the gross lack of information on the subject. This study was designed to evaluate the efficacy of IRS and ITN usage in preventing malaria transmission. Two groups of subjects were interviewed: one from Zanzibar, Tanzania, where both IRS and ITNs are used; a second group from Dar-es-salaam, Tanzania where only ITNs are implemented. The two groups displayed an equal understanding of how malaria is transmitted and how it is prevented. In Zanzibar: 9 males were interviewed, 77% owned a net, and 33% had malaria within the last three years. In Dar-es-salaam: 8 males and 2 females were interviewed, 90% owned a net, and 90% got malaria 1+ times per year. The subjects from Dar also reported about the people living within their home: 33 total people (14 female, 19 male), 96% owned a net and 96% got malaria 1+ times. In addition to gathering quantitative information, a case report documenting one Tanzanian's (in) ability to protect himself from malaria despite preventive efforts is included.

Methods: This study seeks to explore the subjective determinants involved in an individual's perception of malaria. Qualitative research is concerned with information-richness. As a result, sampling is purposive not random. Study participants are valued for possessing a range of experiences characteristic of adults from Tanzania. In keeping with similar published qualitative studies, this study involves two groups: one from the Tanzanian mainland and one from Zanzibar. Transcripts will be analyzed by considering: specific word usage, the context in which a given comment was made, the precision of the responses, and any major themes that emerge from the interview as a whole.

Results: Mainland
- 10 people interviewed
- 80% male
- 90% owned a net
- 90% got malaria 1+ times per year

Zanzibar
- 9 people interviewed
- 100% male
- 77% owned a net
• 33% had malaria at some point in their life

Quotes
• "Malaria is fever."
• "I get malaria once a year during June to August. The medicine lasts for one year, so I first got it in June and then the drugs lasted for one year and then I get it again."
• "I always get malaria in September because it is too cold."
• "My neighbor died at age twenty because he overdosed on Fansidar."
• "I think I will wake up if a mosquito lands so I do not need a net."
• "People die from medicine that has expired so it does not prevent malaria. You cannot be sure."
• "My nephew died from malaria because of late treatment ...he was three years old."
• (What causes malaria?) "Mosquitoes touch you."

Case Study
Many people seem to have access to nets and understand the importance of nets, and yet people still get malaria. As I spent more time in Dar, I feel as if I began to understand the basis of this problem.

First of all, sleeping under a net is not comfortable. I slept under one about half of the time. It was annoying and hot, and I was there in the winter. I cannot imagine it during the rainy hot season. As a young adult, it can be hard to see how harmful a malaria infection is. Most people contract the infection 1-3 times per year. They are sick for 3-7 days, but as long as they take the proper medicines, then they will be fine. What most people fail to see is that every adult that gets malaria increases the risk of a child <5 yo getting infected. Thus, bed nets have a dual purpose, they protect the individual under the net, but they also protect the little baby down the street. During my stay in Dar I bought bed nets to give to people I had met. They are about three dollars each, which is a lot when you only make five dollars a day. Further, malaria infections in young children are hard to identify because they cannot speak. People may not be aware of the true burden of the disease.

I met Sarum while in Dar. He lived in the peri-urban slums surrounding Dar. His corrugated metal room contained six items, as far as I could tell: a bed, a bedside table, a radio, a bag of clothes, a bednet, and insecticide spray. One third of his belongings were dedicated to preventing malaria. I usually met Sarum at his work and we walked to his house. One day he did not show. I found out from his colleague that he was sick with malaria. I was shocked. First I went to the pharmacy to buy medicine. I initially asked for malarone and the pharmacist laughed at me. It was too expensive to buy, so she did not carry it. I bought Sarum a treatment of artemisinin combination therapy, and then realized I had malarone. I then took it all to his house. When I arrived, he was obviously ill: sweating, fever, and miserable. Unfortunately he had already taken a course of sulfadoxine-pyrimethamine so he could not take the other meds. I left them with him for next time. Apparently, his meds were not working because the next day he went to the hospital and got an IV course of SP. There is no way of knowing the quality of the medicine he bought. Sarum recovered, but I was disturbed by the experience. Sarum did all the right things, and he still got malaria. And the best medicines were not even available for him when he needed them. What more can a person do?

The opinion of the principal investigator is that the government should spray insecticides. The majority of people with whom I spoke in Zanzibar and the mainland knew what to do in order to prevent malaria, but the mainlanders got infected much more frequently. There are many differences between Zanzibar and the mainland. The most conspicuous one to me is the presence of insecticide spraying in Zanzibar and its absence in the mainland.
References
Illness in the Field: A Case of Dengue Fever

Objectives: This project details the series of events that occurred when a member of a fieldwork research team in Costa Rica became acutely and severely ill. This forced the students to abandon their project and evacuate the country to seek adequate medical care.

Methods: The project presents the experiences of the students from their individual perspectives, one person's suffering from the illness itself and the other person's observations during that time. Pictures and drawings are employed to help illustrate the situation.

Results: Over the course of 5 days, one of the students involved with the project develop a severe illness, beginning with headache and fever, leading to nightly chills and sweats, loss of appetite, and eventually hallucinations. The other student watched this occur, and had to make difficult decisions regarding where to go, who to talk to, and what to do. Ironically, the students had to access a medical system they were there to study. When he started experiencing symptoms of illness as well, the students decided to return home to the United States for medical care.

Conclusions: Important decisions must be made during times of illness, balancing the desire to continue the research project with the need to maintain one's health and wellbeing. It is also important to consider and plan for circumstances when a team member on a fieldwork project becomes ill, in addition to taking preventative measures before leaving.
Patient Perspectives on Living with Cancer: A Qualitative Study in Costa Rica

Background: Cancer is a major cause of morbidity and mortality in Costa Rica. It is the second leading cause of death after cardiovascular disease, accounting for an estimated 20% of annual mortality in 2003. On an individual level, cancer may radically challenge a patient's identity and profoundly undermine a sense of security. A deepened understanding of cancer patients' experiences during treatment may help physicians and others better meet the emotional needs of these patients. Qualitative research focused on patients' narratives has effectively elucidated common themes in the experiences of cancer patients in the United States and Europe. In our research, we interviewed cancer survivors in San Jose, Costa Rica about the longitudinal experience of their illness. As we collected survivors' illness narratives, we explored their experiences dealing with cancer and the choices they made about their care throughout the progression of their disease.

Objectives: Our intent was to characterize how a small nonrandom sample of Costa Rican survivors approached life with cancer using a qualitative approach centering on patients' narratives. We were particularly interested in how they chose and obtained different sources of care, comfort and treatment. We hoped to explore the evolution of patients' perspectives on their illness throughout the progression from pre-diagnosis through treatment. Through the lens of cancer survivors' experiences, we gained insight into the availability of familial and community support, the use of complementary medicine, as well as administration of conventional medical therapies.

Methods: We interviewed seven cancer survivors (one colon cancer, one thyroid cancer, five breast cancer). Six were female, one was male. Each survivor had been disease-free for at least two years (range 2-22 years). During the interviews, which lasted between one and two hours, we asked patients to describe their experiences of cancer from initial symptoms, if any, through diagnosis, treatment and post-treatment, disease-free life. Patients were recruited through Fundacion para al Paciente con Cancer, a non-profit organization providing supportive services for cancer patients and survivors. We made contact with Fundacion para al Paciente con Cancer via the Costa Rican National Cancer Institute (CRNCI) of which our in-country preceptor, Dr. Estaban Avendano-Fernandez, is director. Our subjects were selected and contacted with Dr. Avendano-Fernandez's guidance; in this, we benefited from his experience in cancer research and working with human subjects. Our translator and cultural liaison was Sebastian Calvo, a second-year medical student at the University of Costa Rica Medical School. Interviews were scheduled at the convenience of the patients.
All subjects received a written document (in English and Spanish) and verbal information in Spanish to ensure informed consent. Eligibility criteria included patients over 18 with a previous diagnosis of any cancer deemed by their physician to be a serious threat to life or health who were now in a disease-free state. Participants were encouraged to ask questions and voice any concerns throughout the interview process, and were explicitly told they could withdraw participation at any time. Each interview began with collection of basic demographic information (age, sex, cancer diagnosis) and then continued with open-ended questions that led the patient through his or her experience. Our goal was to elicit the patient's story of his/her illness and to establish what he or she thought were the most salient points in its course.

All interviews were recorded with a digital recorder, including questions in English and their translation into Spanish, as well as answers in Spanish and their translation into English. Detailed notes were also taken by one or both researchers during each interview. These written notes and portions of the digital recordings were then analyzed by each researcher independently in order to inductively generate common themes or motifs.

Results: Researchers in the US and Europe have frequently found patients quite eager to tell their stories. In fact, enabling patients to construct and give voice to illness narratives has been studied as a therapeutic practice. The cancer survivors we interviewed were likewise quite willing to tell their stories and frequently answered open-ended questions with lengthy elaborations upon their experiences. These survivors were all involved in either formal support groups or in volunteering to counsel newly-diagnosed patients. Thus, they each seemed to have some prior experience telling their stories in other contexts.

Inductive data analysis revealed several prominent themes within the narratives of our seven subjects. While each subject's experience contained numerous distinct elements and unique details, common themes emerged as well. Four themes seemed particularly salient. (1) First, all subjects who had undergone it (6/7) identified chemotherapy as the most difficult part of their treatment, much more trying than recovering from surgery or undergoing radiation therapy. This was a highly noxious component of the cancer experience, and left a lasting, often visceral, memory. (2) Nevertheless, our subjects recalled many positive experiences during their treatment as well; all seven subjects gained strength, encouragement and comfort from other individuals. These individuals were family members, friends, nurses, spiritual group members, and other cancer patients and survivors. Facing cancer and difficult treatment regimens seemed to bring our subjects closer to many people in their lives. (3) A third theme in our study was that our subjects felt faith in God helped them persist in the face of painful treatments, including complying with the demands of chemotherapy which generally involved multiple infusions over many months. (4) Finally, our subjects were frequently moved to reach out to others with cancer and doing so seemed to help them view their own experience, painful and frightening as it had been, as worthwhile and even positive. This impulse to reach out could occur in the form of offering informal assistance, hope and encouragement to others in the community suffering from cancer or it might involve performance of more formal volunteer work with a survivor group. Additionally, simply sharing their stories with family, friends and even strangers, communicating that cancer does not have to be fatal, seemed to help these survivors come to terms with their own experiences.

Conclusions: Our study revealed a variety of common themes in the experience of cancer within seven cancer patients in San Jose, Costa Rica. They felt that:

1. Chemotherapy was the worst part of treatment;
2. Support from other individuals gave them strength;
3. Faith in God helped them persist in the face of painful treatments;
4. Offering help to others helped subjects cope with their own suffering.
Water Handling Patterns and Water Beliefs in Cacha, Ecuador: Foundational Research for a Water Sanitation Intervention

Background: Every year, diarrhea takes about 1.8 million lives, mostly of children in developing nations. This death toll persists despite conclusive evidence that low-technology, low-cost household-level water sanitation interventions can reduce diarrheal incidence, irrespective of concomitant hygiene or sanitation improvements. The most successful water treatment programs have anticipated and addressed barriers posed by cultural, behavioral and health-belief factors.

Objectives: In order to guide an effective water treatment intervention, this study sought to analyze the water distribution system and the local behaviors and beliefs concerning water in the rural Ecuadorian region of Cacha.

Methods: Households were chosen based on availability of the residents and on recommendations by local leaders. Surveys were administered verbally at participants’ homes. Survey items explored water procurement, transfer, storage and treatment practices, beliefs about water quality and its relation to health, and beliefs concerning diarrhea. Responses were categorized and then summarized.

Results: In all, 52 households were surveyed, matching the anticipated sample of 5-6 households in 9 of the 23 communities.

All but one village received their water from the central source for the community, which pipes water from a high-altitude stream, through a central sand filter, and finally to spigots outside each house. While only 44% of households had water available from the spigot every day, no households reported a subjective shortage of water. A total of 96% of households stored water outside the house; of these, 92% used a concrete tank, 68% covered the container and 40% used this water for all consumption and non-consumption purposes. A total of 65% of households had an inside storage container used solely for cooking and drinking; 82% of these had covers. Compared to houses in which the head of household is a skilled laborer, houses headed by an unskilled laborer appeared to be more likely to have inside water storage. A total of 48% of households treat their water by boiling or chlorination before consumption. Households without children were less likely to report that they treated their water before consumption. In general, water treatment and safety behaviors appear to vary between communities, but have some consistency within each community.

While 53% of households believed they have clean water, 92% wanted cleaner water. Among the 29% of respondents with ideas about how to improve water quality, boiling, chlorination and improved storage were mentioned with equal frequency. 37% of respondents did not know of any diseases that dirty water could cause.
With respect to diarrheal disease burden, 69% of respondents agreed that diarrhea is a problem in Cacha, and almost one quarter of respondents knew of a child who had died from diarrhea. Several respondents suggested preventative methods to remedy the problem of diarrhea in Cacha, yet the most common idea espoused was seeking as-needed treatment by a physician.

**Conclusions:** Cacha's water distribution system provides adequate water volumes, yet inadequate storage and treatment practices allow down-stream contamination. As such, a point-of-use water sanitation intervention would best serve this community. Implementation should utilize the existing intra-community communication systems, the awareness of diarrhea as a problem and the desire for cleaner water. Lack of understanding about the outcomes of unclean water and the value of prevention must be addressed.

**References:**


Reticence to seek HIV/AIDS testing in high-risk women of the Dominican Republic

Objectives
The overall prevalence of HIV/AIDS has stabilized in the Dominican Republic; however, the incidence of the disease in women between the ages of 18 and 49 is on the rise. Although significant funding has been provided to the country to implement prevention initiatives to combat the disease, it is widely recognized that stigmas toward HIV/AIDS frequently hinder prevention measures. Our research attempted to identify factors that may prevent women from seeking HIV/AIDS testing, which can ultimately limit the success of prevention programs. Furthermore, we assessed differences in the barriers that thwart efforts to seek HIV tests between female residents of inner city Santo Domingo and of the sugarcane plantation communities (bateyes).

Methods
Women between the ages of 18 and 49 were eligible to participate in our comparative study, and participants were grouped either as residents of the bateyes or of inner city Santo Domingo. An oral Spanish-language survey was performed to measure the influence, on a zero (“I don't know”) to five (“Major influence”) scale, that employment, healthcare, and social-related factors would have on the decision to seek HIV testing. Responses were evaluated using ANOVA single factor analysis and considered statistically significant only if they yielded a p-value below 0.05.

Results
A total of 104 women from the bateyes (Dominican descent 56.7%, Haitian descent 17.3%, mixed ethnicity 24.0%, no response 1.2%) and 117 women from inner city Santo Domingo (Dominican descent 91.5%, Haitian descent 5.13%, mixed ethnicity 3.42%) were interviewed. 84.6% (n=99) of women in the inner city reported having had a prior HIV test, as compared to 79.8% (n=83) of the women in the bateyes. There were no significant differences between the two comparative groups for any specific factor that might prevent a woman from seeking HIV testing. However, the most important factors in both the bateyes and inner city Santo Domingo were social-related fears (average categorical ranking: bateyes, 2.7 and city 2.6, p-value <0.05 respectively).
Conclusion
Our findings suggest that discrimination of women by their communities, regardless of where these communities are located, plays a larger role in their decision to seek testing than fears related to employment or reduced health-care access. This indicates that HIV test promotion would potentially be more effective if centered around reduction of both intimate partner violence and community-based stigma towards individuals affected by HIV/AIDS.

References

Abstract:
The HIV epidemic is a major global health challenge. The Joint United Nations Program on HIV/AIDS (UNAIDS) reported that in 2004, 3 million people worldwide died of AIDS and an estimated 5 million people acquired HIV. Studies in animal models and observational data from humans suggest that cell-mediated immune responses may be key to controlling HIV infection. MRKAdS HIV-1 gag/pol/nef, a clade B-based adenovirus serotype 5 HIV-1 vaccine, has been shown to elicit T-cell mediated immune responses. The vaccine appears to be safe and generally well tolerated in previous Phase 1 and 2 studies in HIV uninfected people. The purpose of this study is to evaluate the safety and efficacy of the MRKAd5 HIV-1 gag/pol/nef vaccine in HIV uninfected participants from South Africa, where clade C is predominant. The study will address whether a clade B-based vaccine designed to elicit T-cellular immunity will demonstrate efficacy in reducing acquisition of infection, or reducing HIV viral load in persons who become infected in a non-clade B region.

Objectives:
• Acquisition of HIV-1 infection
• Viral load set point (HIV-1 RNA at approximately 3 months post diagnosis) in study participants who become HIV infected

Methods:
This study will last about 4.5 to 5.5 years. Participants will be randomly assigned to receive 3 doses of either vaccine or placebo. All participants will receive their injections at study entry and at Months 1 and 6. Participants will be asked to complete a post-vaccination symptom log for the 3 days following each vaccination to monitor body temperature and symptoms known to be associated with the vaccine. At all study visits, participants will be asked about any adverse events they may have experienced. There will be at least 14 study visits over the first 4 years of the study. A physical exam, medication history, risk reduction counseling, and blood collection will occur at every visit. Participants will be asked to complete a social impact questionnaire at Weeks 12, 78, and 208; an outside testing and belief questionnaire at Weeks 30, 78, 130, 182, and 208; and a circumcision status assessment at Week 208. Participants will undergo HIV testing to check their HIV status approximately every 6 months. Additional visits will be required for any participant who becomes infected with HIV during the study.
Factors Influencing Adherence to Treatment and Barriers to Care for HIV-Positive Individuals in Santiago, Dominican Republic.

Abstract: The Caribbean basin has the second highest prevalence of HIV/AIDS in the world, with 75% of the cases localized to the Dominican Republic and Haiti. Despite recent efforts to implement more effective treatment programs, AIDS-related deaths persist as the leading cause of mortality in the region. Barriers to accessing and maintaining healthcare for HIV/AIDS are constructed through an array of complex interactions between socioeconomic factors which may include: AIDS-related stigma, discrimination, insufficient resources, personal and cultural belief structures, and the complexity of pharmacotherapy. This study was designed to assess and evaluate the specific barriers to care and adherence to treatment in Santiago, Dominican Republic, through survey data collected from both HIV positive patients and clinic healthcare providers. In addition, the issues identified in Santiago were compared to a control population in Rochester, N.Y to help assess relative deficiencies in care. This study provides valuable information to aid in the implementation of future strategies to augment patient compliance and access to care in Santiago.

Objectives: The two primary objectives of this study were as follows: (1) to investigate the major factors that impede patient adherence to treatment and care at the Clinica de Enfermedades de Immunologia (CEDI) in Santiago, Dominican Republic, and (2) to compare these issues to a control group from the AIDS Center adult clinic at Strong Memorial Hospital in Rochester, NY to identify relative discrepancies in care between the two sites.

Methods: Study data was collected through a survey given to patients at the Santiago clinic. HIV patients in a control group in Rochester, NY, were given the same survey and their responses were compared with results from Santiago.

Results: The major differences identified between the clinics were why patients sought HIV testing, the percent of patients seen at the clinics currently treated with HAART, and the support systems patients relied on. Over 65% of patients in Santiago were tested for HIV only after being symptomatic or sick, whereas in Rochester over 50% were tested because they felt they were at risk. Regarding resources, the clinic is the primary place in Santiago that provides services and care related to HIV, and 90% of patients rely on it for major support. In comparison, Rochester has other organizations that provide support to patients, and only 65% of patients rely on the clinic for support beyond medication. Finally, all HIV patients at the Rochester clinic were actively receiving HAART, while in Santiago 10% of patients were not receiving any antiretroviral therapy.
Conclusions: Differences in the quality of care provided between the clinic in Santiago and in Rochester are primarily a function of the limited availability of resources in Santiago. There were insufficient quantities of antiretroviral medications available for patients, personnel available for providing care, and other services such as education and case management at the clinic in Santiago as compared to the clinic in Rochester. Developing strategies to augment the quality of care for HIV patients in Santiago should focus on addressing the issues identified in this study.

References:
UNAIDS Executive Summary, 2006.
Binding Phenotype of Parasites Causing Severe Malaria:
The Search for a Vaccine in Tanzania

Abstract: Every 30 seconds a child in sub-Saharan Africa dies from Malaria infection. The majority of these deaths are attributable to severe malaria syndromes. *Plasmodiumfalciparum* exerts its pathogenesis via variant surface antigens (VSA) expressed on the outside of the infected red blood cell that allow binding of the parasite to host cells. In parasites causing pregnancy malaria, VSA mediate binding to Chondroitin Sulfate A. It is hypothesized that parasites causing severe malaria, like parasites causing pregnancy malaria, will bind to a particular molecule. This molecule could serve as a vaccine target against severe malaria.

Objectives: To determine if the binding phenotype of *Plasmodiumfalciparum* parasites is related to the clinical syndrome that those parasites cause.

Methods: The study took place in Morogoro, Tanzania. Subjects were children under the age of five recruited through any of three studies underway with Mother-Offspring Malaria Studies (MOMS). The clinical course of the children was monitored by study physicians. Blood samples were taken from children infected with *Plasmodium falciparum*. The parasite was cultured until it reached the trophozoite stage. Binding assays were used to assess binding to thirteen molecules. Statistical analysis was performed using JMP version 6.0.2, 2006.

Results: The clinical experience of 96 of the children was known. Of these children, 66 (68.8%) experienced severe malaria. Twenty children had severe anemia, 44 had respiratory distress, and 30 had cerebral malaria. Binding assays performed showed that parasites that bound Laminin were significantly likely to come from children who experienced respiratory distress. Conclusions: Severe malaria is a significant problem in Tanzania and this region, in particular. The relationship between parasites that bind laminin and respiratory distress suggests that binding to laminin may mediate the respiratory distress syndrome. However, the number of parasites binding to laminin was low. Further delineation of the relationship is suggested.

References:
Fried MF and PE Duffy (1996). Adherence of *Plasmodiumfalciparum* to chondroitin sulfate A in the


http://www.who.int/malaria/docs/TreatmentGuidelines2006.pdf

Palliative Care in Hong Kong: Effectively Providing Comfort & Care during the Last Months of Life?

Abstract:
Although pediatric deaths occur much less frequently than adult deaths, millions of children worldwide still die every year from life-threatening medical conditions. In the past, this area has been vastly understudied. The pediatric palliative care system in Hong Kong was started in 1997 as collaboration between the Hong Kong Hospital Authority and the Children's Cancer Foundation. As a result, the current system continues to only serve children with terminal cancer. This study interviewed the parents of 15 children with terminal cancer who were currently receiving palliative care or who had recently died while receiving palliative care to evaluate both the strengths and weaknesses of the current system. Based on the experiences of parents in this study, the pediatric palliative care system in Hong Kong is effectively addressing the medical, psychological, and spiritual needs of children with terminal cancer and their families.

Objective:
- Identify both the strengths and weaknesses of the current pediatric palliative care system

Methods:
This study included the parents of fifteen children with terminal cancer who were currently receiving palliative care or who had recently died while receiving palliative care. All parents were selected at random according to all factors. The Children's Cancer Foundation (CCF), the foundation that runs the pediatric palliative care home service in Hong Kong, explained the study and that participation was voluntary to each family. If the family agreed to participate, the CCF provided the contact information to the PI. The PI then contacted each family to review the study information letter and conduct interviews. All interviews were conducted in the family's first language using a translator.

Results & Conclusions:
Since the pediatric palliative care system in Hong Kong was started ten years ago, no studies have examined how effectively the system provides medical, psychological and social support for the terminally ill children and their families who utilize the system. Overall, parents were satisfied with all aspects of their child's palliative care experience. One area that parents were particularly satisfied with was the care that the doctors and nurses provided. Families said that the medical providers were "helpful, cooperative, caring and understanding" throughout the entire process. The second area that parents were most satisfied with was the psychological support provided by the Children's Cancer
Foundation. Families were grateful that foundation nurses were always available during home visits to answer questions, sort out any problems and serve as a source of emotional support for both the child and family. Although most parents were satisfied with their child's spiritual and psychological care, their suggestions for improvement in this area included play therapy for the child and more frequent visits from the hospital chaplain. All of the services that parents discussed are only available to terminally ill cancer children. Expansion of the pediatric palliative care system to serve all terminally ill children is one area for future improvement. This study provides qualitative data to serve as a baseline for future research on pediatric palliative care in Hong Kong.

References:
Healthcare Availability and Accessibility in Rural and Urban Madagascar

Abstract: Madagascar is the 11th-poorest country in the world. With a WHO-estimated gross per capita income of $880 (approaching $0 in rural areas where subsistence farming is the norm), a staggering number of people cannot afford basic healthcare. In remote regions, the principal, and often essentially only, source of healthcare is international aid.

Objectives: We sought to observe and qualitatively compare rural and urban healthcare availability.

Methods: As three American medical students in Madagascar, we observed and took part in healthcare in the rainforest villages surrounding Ranomafana National Park (RNP) and in Fianarantsoa, Madagascar's 3rd-largest city. We visited the rainforest villages with a Malagasy health educator employed by RNP's biological and ecological research station (there were not currently any physicians or nurses employed by the station). Our village visits focused on education: hygiene, care for the sick, medical emergency recognition, etc.; however, we also distributed malaria treatment, water treatment, and over-the-counter medications (there were none in most villages) and provided basic medical care and advice to the acutely ill. Subsequently, we shadowed infectious disease doctors and surgeons in the city of Fianarantsoa.

Results: During question-and-answer periods following our village education sessions, we noted the striking lack of even the most basic medical knowledge and the essential absence of access to medical care. In Fianarantsoa, we were impressed by the level of care offered in the public hospital.

Conclusions: We departed Madagascar convinced that adequate healthcare is at least available in Madagascar's largest cities for those who can afford it, but that there is a huge need for health education and basic, intransient healthcare infrastructure in remote regions.

References
Choledochal Cysts: a 10 year experience in Northern India

Abstract:
A retrospective review of patients with choledochal cysts seen at All India Institute of Medical Sciences (AIIMS) in New Delhi, India between 1995 and 2005 was conducted. 28 patient charts were reviewed. Age, sex, diagnosis (by HIDA scan and ultrasound), cyst type, presentation, physical examination findings, procedure type, and liver function tests for each patient were recorded. Sufficient follow-up data was available for 10 patients; in these patients school attendance, quantity of food eaten in one sitting, discomfort after fatty food ingestion, abdominal pain or distension, episodes of vomiting or jaundice, change in hunger or weight, episodes of unexplained fever, and presence of blood in stool was used to gauge post-operative well-being. Of these patients, only 1 complained of abdominal pain and was successfully treated for constipation. Hepaticojejunostomies are usually preferred, and the benefits are well documented. In the minority of patients that require hepaticoduodenostomies, the outcomes are also favorable, despite limited resources.

Objectives:
- Report the post-operative outcomes of hepaticojejunostomies versus hepaticoduodenostomies performed on pediatric patients with choledochal cysts.

Conclusions:
Hepaticoduodenostomies are done in acute cases with friable cysts, or the presence of cysts in the lower portion of the CBD with a normal upper portion. In the vast majority of patients, hepaticojejunostomies can be accomplished, and the benefits are well documented. In the minority of patients that require hepaticoduodenostomies, the outcomes are favorable. With limited follow-up data we can say that these patients are doing well, despite the limited resources. With more thorough record keeping in the future, we hope to continue studying patient outcomes.

Our data shows a slightly higher predominance of males with choledochal cysts, as compared to other studies. This is most likely due to the fact that in the male dominated society in which this study was conducted, males are brought to medical attention earlier. Clay stools presented more commonly in patients less than 1 year, and were the earliest sign of obstructive jaundice.
References
Assessment of Instrument Sterilization Efficiency in Developing Countries: Observation of Material Use and Processing in the Ob/Gyn Department of Hospital #51 of Durango, Mexico

Objectives: Nosocomial or hospital-acquired infections can result from inadequate application of aseptic techniques or sterilization methods and can lead to unnecessary morbidity and mortality. The purpose of this study was to investigate the effectiveness of the different medical instrument sterilization methods available to a country with limited resources. The study was conducted in the Department of Obstetrics/Gynecology (OB/GYN) in the General Hospital de Durango #51 in Gomez Palacio, Mexico. The project involved an observational investigation of the methods used for sterilization and storage of equipment utilized in the management of patients before, during, and after medical care in the OB/GYN department. Variables observed include: the method of implementation of foley catheters used during procedures, sterilization of the operating room before and after a procedure, storage and sterilization of fabric and instruments used during the procedures (i.e., cesareans, hysterectomies). Also, the sterilization practices were investigated and compared to the hospital protocols in order to assess adherence to the protocols and the extent of variation among health care personnel.

Hypothesis: We hypothesized that there would be great variability in the sterilization methods of the operating rooms and of the patients; and that there would also be variability in the catheter implementation methods. In addition, we expected to find accommodations made in the hospital as a result of having limited resources.

Methods: Over a period of 4 weeks, observations were made on the sterilization methods of 18 hospital personnel (8 physicians, 4 sanitation workers, 6 nurses), and the observation of the catheter implementation technique of 22 patients was also completed with routine urine analysis checks for assessment of possible contamination. All patients receiving a catheter for surgery preparation in the OB/GYN department were eligible for inclusion in this study given that they had neither a history of UTI nor presence of blood in urine. Currently at the Hospital #51, it is assumed that sufficient sterilization methods are upheld by the health care personnel, but in some instances such as catheter implementation, there is no set hospital protocol.

Results: The departments and areas of the hospital observed include: the surgical floor of obstetrics and gynecology, the Obstetric Inpatient Hall, the Receiving department of Hospital
Materials, the Warehouse, the department of Basic Services (including Septic rooms), the General Laundry Plant of Torreon, and the department of Exploration & Preparation. Despite the fact that the Department of Basic Services had a protocol, a great degree of variability was found among the various sterilization methods of the personnel. The variability among the janitorial staff was more apparent with sterilization methods of the operating room; there was significantly less variability in methods over time when the staff was not working independently, in locations such as the General laundry plant of Torreon, and the department of Exploration & Preparation. There was little variability in the method of catheter implementation among the nurses. Blood was found in the urine 11 out of 22 cases however, which may suggest contamination during those trials. Differences in the storage conditions were also found. The cabinets containing instruments ready for surgical use had cabinet doors and were elevated from the ground (between the recommended 8-18cm) with little crowding on the shelves; whereas the cabinets used for long-term storage, or easy access of materials in case of emergency, did not have doors, were more crowded, and the lowest shelf was at times only 1 inch above the floor. The materials on all shelves were packaged, although the packaging ranged from cloth to paper with tape depending on the instrument. Although the sterile spaces were respected in the hospital by the clothing worn in the various departments observed and demarcations indicating sterile environments, there were also significant phenomena observed that would inhibit the ability to achieve a truly sterile operating room environment (such as the method of storage of the disinfecting agents, ventilation, disposal of soiled material, etc.).

Conclusions: The great variability found in some of the areas of sanitation control demonstrated that there is a need for a more duly enforced hospital protocol in those areas. In addition, when cleaning faculty members were working in the presence of others, the protocol was followed more uniformly among the personnel. This would support the suggestion that the protocol might be followed more closely if more than one person were to clean the operating room at a time. Other areas of the hospital took great precaution to maintain sanitation protocols, however some of the common scenes in the operating room, including the disposal soiled materials, impede the ability to maintain a truly sterile environment, and thus the hospital should benefit from a review of such positive and negative findings.

References:
Underground Medicine: St. Joseph's Neighborhood Center and Rochester's Uninsured

Abstract:
After filming various individuals involved with different aspects of healthcare in Rochester, we put together a film in order to offer a window into healthcare for Rochester's uninsured, as well as some of the issues concerning physicians practicing in Rochester. St. Joseph's Clinic was the approach to uninsured healthcare that we focused on; St. Joseph's has not only been extremely successful in providing care and reaching those in the community that would otherwise have no source of healthcare for any number of reasons. Both physicians and administrators shared common opinions on the efficacy of St. Joseph's as well as common concerns on the direction and future of healthcare in general in our community. By allowing physicians to choose what they would like to do, their own goals for their time there, and how they would like to accomplish that, St. Joseph's has been very effective in retaining physicians, all of which are on a volunteer basis. Also their leniency and catering to physician requests/needs, the clinic has a surprising capacity to offer specialty services to patients in order to offer assistance in all facets of well-being. The general consensus in regards to St. Joseph's seems to be that it could serve as a prototype for healthcare relief for the uninsured, but also as a model approach towards healthcare in general. St. Joseph's has caught the attention of not only local leadership, but also that of the other prime healthcare providers for our community.
We also gathered thoughts about concerns physicians in Rochester have, and reasons why so many physicians chose to leave Rochester. Physicians and those in leadership positions all conveyed similar thoughts; insurance costs, increasing commercialism in regards to medicine, and a generalized drop in the collaborative spirit that the Rochester medical community has been known for, all contribute to physicians' dissatisfaction in our community.

Objectives:
- To examine opinions on the state of healthcare for the uninsured in Rochester, as well as one approach of its management.
- Examine local doctors' concerns and causes for dissatisfaction for practicing their profession in the Rochester community.
- Compile information and opinions on healthcare in Rochester in a format that is easily accessible and has a higher likelihood of reaching an audience outside of physicians alone- as a documentary.

Methods:
- Interviewing administrators at St. Joseph's Clinic, healthcare leaders in Rochester and representatives of physicians in Rochester, as well as local physicians themselves.
Results:

- All physicians interviewed had varying years of time at St. Joseph's but all agreed on its efficacy and extreme success in treating those that would otherwise not have access, as well as those who would otherwise have not sought healthcare.

- Physician concerns about healthcare in Rochester are similar to healthcare issues on a national basis regarding insurance for patients and to practice, cost of care, and a rising competitive rather than collaborative drive in medicine. However these concerns are in some ways unique to Rochester since in years past Rochester was known for its tight knit medical community that shared an overall driving goal of providing the highest quality healthcare to this community as possible.

Conclusions: A volunteer based model of healthcare serves to help underserved populations in Rochester currently and will continue to be viable as volunteerism expands but this is a temporary solution to a larger problem in our healthcare system. Rochester physicians' level of satisfaction has clearly decreased and some of their concerns are very specific and seemingly universal. The specificity of these concerns would makes the development of goal-oriented plans, directed at increasing satisfaction with practicing medicine in Rochester, feasible.

References -
Interviews with Nancy Adams, Bonnie Devinney, Warren Glaser, MD, Louis Papa, MD, Lindsay Phillips MD, and Chris Wagner, SSJ.


LQTS: Clinical Course and Risk Stratification in Subjects Genetically Tested for the Congenital Long-QT Syndrome After Age 40 Years

Abstract: The overall purpose of this longitudinal prospective study is to assess the cumulative risk of cardiac events in genetically identified Long-QT Syndrome (LQTS) subjects from age of 41 years through 60 years (20-year follow-up period). Characterization of the clinical course of LQTS is well described from birth to age 40 years. This contingency analysis of LQTS is clinically important for survivors who live over the age of 40. In addition, therapeutic interventions proven to reduce risk of cardiac events in teenage and adult years permit affected LQTS subjects to reach 40 years of life. As a consequence, further evaluation of genetically affected LQTS patients need to be assessed to determine whether risk of cardiac events in this population persist into middle age years.

Objectives: (1) To examine differences in risk for all-cause mortality and aborted cardiac arrest in genotyped positive subjects in comparison with genotyped negative LQTS subjects between 41-61 years (primary outcome); (2) To compare the risk for aborted cardiac arrest or death in LQT1, LQT2, and LQT3 populations between 41-61 years; (3) To identify risk factors for syncope, aborted cardiac arrest or all-cause death after age 40 years within genotype positive LQT1, LQT2, and LQT3 subjects; (4) To evaluate the efficacy of reducing cardiac events with currently used P-blocker therapy after age 40 years.

Methods: This study comprise of subjects who are enrolled in the International Long-QT Syndrome Registry. The Kaplan-Meier life-table method will be used to assess the time to a first life-threatening event and the cumulative event rates by genotype negative, genotyped positive, and LQT1, LQT2, and LQT3 subgroups; risk stratification subgroup analyzes will then be performed. The results will be compared using the log-rank statistic. Multivariate Cox proportional hazards regression modeling will be used to assess the independent contribution of each factor to the development of ACA or death from age 41 years to 61 years. Pre-specified factors in the multivariate models will include gender, QTc category (based on pre-specified second and third quartile cutoffs), and prior history of syncope (defined as transient loss of consciousness that was abrupt in onset and offset). The occurrence of syncope will be evaluated in a time-dependent manner. In addition, the efficacy of P-blocker therapy will be evaluated in a time-dependent manner. These analyzes mentioned above will be repeated using the secondary endpoint of syncope, ACA or death.

Results: Genotyped positive subjects had a significantly higher cumulative rate of ACA or death compared with negatively genotyped subjects (7.1% vs. 1.6% respectively; p=0.005). A QTc value above 490msec was predictive of ACA or all-cause mortality (HR= 5.78, p=0.006). LQT3 was associated with a significant 7-fold increase in risk of ACA or death as compared to genotype negative subjects (HR=6.91, p=0.016) and a significant 5-fold increase in risk as compared to LQT1 subjects (HR=5.05, p=0.01). Genotype positive subjects, as compared to genotyped negative subjects, continue
to have an increase cumulative risk of cardiac events (16.4% vs. 5.1% respectively, p<0.001). Prior history of syncope (HR= 2.73, p<0.001) and the third QTc quartile (HR= 2.52, p=0.015) were predictive of cardiac events. LQT2 subjects have the highest cumulative cardiac event rate compared to LQT1, LQT3, and genotype negative subjects (22.6%, 12.1%, 15.4%, and 5.1%, respectively).

Risk reduction in cardiac events from use of β-blockers in LQT1, LQT2, and LQT3 subjects resulted in an insignificant risk reduction ranging from 19-43%.

Conclusions: LQTS continues to significantly contribute to the risk of events between 41-60 years. Risk factors in this older age group include QTc duration, a history of syncope and the presence of the LQT2 and LQT3 genotype in genetically tested individuals.

References


Damon City Campus Wellness Center Serves as a Health Resource for Students

**Background:** In Spring 2006, the Damon City Campus (DCC) of Monroe Community College (MCC) opened the DCC Wellness Center in order to provide non-medical, health-related services for DCC students. The vision is that the Wellness Center will support students in becoming healthy and successful college students with the confidence and energy to live each day to its fullest by developing a personalized approach to healthy living which encourages self-responsibility and community health. To support the Wellness Center vision, programs and events were developed based on four target areas: assessment, education, self-advocacy, and access to services.

**Methods:** The number of students attending Wellness Center events was tracked using a counter. For assessment, health screenings and HIV testing were offered, and self-care brochures regarding a variety of topics such as diabetes, STD's, etc. were placed out for students. We also electronically administered the National College Health Assessment (NCHA) survey to random full-time DCC students to determine priority health issues among the student population and to develop future programs and events based on those results. For education, various health awareness events and activities were held, including a pledge to quit smoking and a workshop on nutritious meal planning for children. For self-advocacy, a service-learning health class was charged with researching and presenting health topics to fellow students at the annual Wellness Fair. For access to services, brochures on various community health agencies were held in the Wellness Center along with more information on what medical services are offered to students through the MCC health center.

**Results:** From September 2006 to April 2007, a total of 406 students, staff, and faculty visited the Wellness Center and attended the activities and events. For the NCHA survey results, a total of 154 students responded, a response rate of 22.95%. The average age is 27.59 years old. Most are female (72.7%) and heterosexual (88.4%). The majority is non-white (39% Black, 11% Hispanic, 9.1% Other, 1.3% Asian). The demographics are comparable to those of the DCC student population. The areas that were most striking and concerning to us were depression, violence, sexual behavior, tobacco use, and obesity. For depression, within the last 12 months, over half (52.6%) of the respondents have experienced some level of depression, and over one-fifth (22.8%) have considered or attempted suicide. For violence experienced within the past 12 months, almost a third (32.9%; 38.7% F, 15.8% M) of the respondents were involved in an emotionally abusive relationship and almost a third (27.7%; 24.4% F, 31.6% M) either were involved in a physical fight or were physically, non-sexually assaulted. For sexual behavior, over two-fifths (41.6%) of the respondents or their partners did not use any sort of birth control method the last time they had vaginal intercourse. For tobacco use, almost a third (28.1%) of the respondents have smoked cigarettes daily for the last 30 days. For obesity, almost half (47.8%) of the respondents are considered overweight or obese based on their BMI.
Conclusion: The Damon City Campus Wellness Center serves as an important health resource for students. Many came to visit the Wellness Center, attended the events, and participated in the activities. For the next year, the Wellness Center will be developing programming focusing on depression, violence, sexual behavior, tobacco use, and obesity.
Deep Vein Thrombosis Surveillance Patterns in the National Trauma Data Bank: The More We Look, the More We Find

Background: Deep vein thrombosis (DVT) has been identified as a marker of quality of care by various governmental and consumer groups. However, the lack of standardized DVT surveillance systems across trauma centers may introduce bias in the rates of DVT reported. We hypothesize that trauma centers with higher rates of duplex ultrasound screening detect more DVTs and subsequently report higher DVT rates to the NTDB.

Methods: We queried the NTDB version 6.1 and calculated duplex ultrasound rates and DVT rates per trauma center. We examined the relationship between the number of duplex ultrasounds performed and the number of DVTs reported per hospital. In order to account for variability in data reporting, we excluded hospitals that did not report performing any ultrasounds as well as hospitals that did not report any complications. Of the 700 facilities in the NTDB, 147 met these criteria (21%), accounting for 578,252 patients (39% of the total patients in the dataset). A simple linear regression was used to describe the association between ultrasound and DVT rates among hospitals.

<table>
<thead>
<tr>
<th>Duplex Ultrasound Rates</th>
<th>Relative Increase</th>
<th>95% Confidence Interval</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 Duplex/100 Patients</td>
<td>0.998</td>
<td>0.95 to 1.05</td>
<td>0.53</td>
</tr>
<tr>
<td>≥2 Duplex/100 Patients</td>
<td>1.073</td>
<td>1.04 to 1.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trauma Designation (N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Level 1 (64)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Level 2 (54)</td>
<td>1.002</td>
<td>0.99 to 1.11</td>
<td>0.49</td>
</tr>
<tr>
<td>Level 3 (8)</td>
<td>1.002</td>
<td>0.88 to 1.21</td>
<td>0.49</td>
</tr>
<tr>
<td>Unknown (21)</td>
<td>0.925</td>
<td>0.81 to 1.05</td>
<td>0.87</td>
</tr>
<tr>
<td>Teaching Status (N)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>University (47)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Non-Teaching (14)</td>
<td>0.983</td>
<td>0.86 to 1.11</td>
<td>0.61</td>
</tr>
<tr>
<td>Community (43)</td>
<td>0.970</td>
<td>0.88 to 1.07</td>
<td>0.71</td>
</tr>
<tr>
<td>Unknown (43)</td>
<td>1.111</td>
<td>0.96 to 1.32</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Results: For every 1% increase in ultrasound rate there is a 0.14% increase in DVT rate reported (95% CI: 0.121- 0.158). After separating the hospitals into quartiles by duplex rate, the DVT rate in the highest quartile was 7-fold higher than the average combined DVT rate in the first three quartiles (1.52% vs. 0.22%, p<.0001).
Conclusions: More aggressive screening procedures may be associated with higher DVT rates. Trauma centers that screen more and report higher DVT rates may be falsely labeled as having decreased quality of care. Using DVT rate alone as an independent quality measure should be reevaluated due to the potential for surveillance bias.

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Year-Out Research

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Hazards of Benchmarking Complication Rates with the National Trauma Data Bank: Numerators in Search of Denominators

Background: Complication rates after trauma may serve as important indicators of quality of care. Meaningful performance benchmarks for complication rates require reference standards from comprehensive and systematically collected data. We examined the suitability of the NTDB as a reference for benchmarking trauma center complication rates.

Method: We selected the 5 most common complications in the NTDB v. 6.1. We used chi-square to compare three rates for each complication using three different denominators.

A) All patients from all 700 reporting facilities as the denominator (n=1,466,887)
B) Only patients from the 441 hospitals reporting at least one complication (n=1,307,729)
C) Patients from hospitals reporting at least one occurrence of each specific complication, giving a unique denominator for each complication (n range= 869,675 to 1,167,384).

Results: There was a 12.2% increase in the rate of each complication when patients from facilities not reporting any complications were excluded from the denominator (p < 0.001). When rates were calculated using a unique denominator for each complication, rates increased 25%-70%, (increase A to C, all p <0.001) and produced a new rank order for the top 5 complications.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Frequency</th>
<th>RateA %</th>
<th>RateB %</th>
<th>RateC % (n=denominator)</th>
<th>Increase A to C %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Comp</td>
<td>64,270</td>
<td>4.381</td>
<td>4.915</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>18,207</td>
<td>1.241</td>
<td>1.392</td>
<td>1.559 (n=1,167,384)</td>
<td>25.6%</td>
</tr>
<tr>
<td>UTI</td>
<td>14,818</td>
<td>1.010</td>
<td>1.122</td>
<td>1.391 (n=1,065,433)</td>
<td>37.7%</td>
</tr>
<tr>
<td>ARDS</td>
<td>6,328</td>
<td>0.431</td>
<td>0.483</td>
<td>0.576 (n=1,098,257)</td>
<td>33.6%</td>
</tr>
<tr>
<td>DVT</td>
<td>5,610</td>
<td>0.382</td>
<td>0.428</td>
<td>0.536 (n=1,047,594)</td>
<td>40.3%</td>
</tr>
<tr>
<td>MI</td>
<td>5,192</td>
<td>0.350</td>
<td>0.393</td>
<td>0.597 (n=869,675)</td>
<td>70.6%</td>
</tr>
</tbody>
</table>

Conclusion: There is great variability in complication data reported in the NTDB. This creates a challenge for appropriately abstracting and interpreting information, especially for performance benchmarking. We recognize the value of the information in large registries, but assert that investigators must take care when selecting appropriate numerators and denominators for their analyses to ensure validity.
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Year-Out Research

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Preceptors:
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The Benefit of Adjunctive Supportive Housing in the Treatment of Eating Disorders: An evaluation of symptom resolution and quality of life improvement

Objective: Evidence-based research into eating disorders is still in relatively early stages of development as compared to research into a multitude of more commonly studied illnesses. Therefore, there is still a lack of studies looking at many facets of these diseases and treatments. Of particular concern is the lack of literature examining quality of life as an indicator of success in recovery. It is of vital importance to examine patient outcomes not only through the objective lens of symptom management, but also through the subjective lens of patient satisfaction and happiness. Another concern we wanted to address is the lack of programs and therefore the lack of literature regarding supported housing as utilized in the treatment of eating disorders. Supported housing is a well evidenced adjunct to treatment of many psychological illnesses, including chemical addiction and schizophrenia, which allows patients to live in safe residential settings in order to support recovery efforts and practice the living skills they learn in treatment. Here in Rochester, Sage House is a location where adult women have recently been able to utilize supportive housing during their treatment. The focus of our ongoing research is to 1). Examine quality of life in addition to symptom reduction as two inextricably important aspects in the evaluation of patient outcomes and 2). Examine how supported housing in concert with partial hospitalization affects these outcomes.

Methods: We followed two groups of women over the age of 18 who were receiving treatment for an eating disorder at the Unity Eating Disorder Partial Hospitalization Program (EDO PHP) at Unity/St. Mary's Hospital in Rochester. One group of 17 women elected to stay at Sage House during their participation in the PHP while the other group was composed of 19 women who were recommended by staff at EDO PHP to stay at Sage House but who elected not to do so. We administered several questionnaires to these women first at admission and then at discharge from the program. All measures were self-assessments administered by graduate students, with the exception of assessment of concrete symptoms (weight, number of binges/purges per week) which were extracted from intake interviews conducted by eating disorder professionals on staff at the partial hospitalization program. The measures used to evaluate outcome of treatment fell into two categories: measures of eating disorder pathology (signs and symptoms) and measures of quality of life.

Results: Both groups of women were found to have both decreased pathology and subjectively increased quality of life. Unfortunately, time constraints prevented us from completing a statistical comparison of the two groups on these measures to determine whether a true difference in outcome was achieved by those who stayed in supported housing. This analysis will be part of a later study. However, an overall greater number of measures and subcategories of measures indicated statistically significant improvement in eating disorder symptoms, attitudes, behaviors and quality of life in the group of patients who stayed at Sage House.

Conclusions: Our findings support the hypothesis that supported housing aids in a better response to treatment in eating disorder patients as measured by both standard tools designed to evaluate signs and symptoms of eating disorders and tools intended to evaluate quality of life.
ACKNOWLEDGEMENTS

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