



SCHOOL OF
**MEDICINE &
DENTISTRY**
UNIVERSITY *of* ROCHESTER
MEDICAL CENTER

Medicine of the Highest Order

2006

Annual Medical Student
Abstract Journal

Sponsored by:

Center for Advocacy, Community Health, Education and Diversity

Offices for Medical Education

Basic Science and Clinical Research Faculty Advisory Committee

Community Outreach Faculty Advisory Committee

International Medicine Faculty Advisory Committee

Medical Humanities Faculty Advisory Committee

Basic Science/Clinical Research

C. Nicholas Eisenhauer IV, MS2

Preceptor:

Glynis Laing, Ph.D.

Manager of Clinical Research Cleveland Clinic

Thoracic and Cardiovascular Surgery

Gender Differences in Postoperative Outcomes of Radiofrequency Ablation for Treatment of Atrial Fibrillation

Introduction: Atrial fibrillation (AF) is a significant contributor to cardiac morbidity and mortality. Surgical procedures have been developed for treatment of AF and several studies have looked at risk factors associated with the recurrence of AF after these procedures. This study will examine the effect of gender on recurrent AF and other post-operative outcomes after successful bipolar radiofrequency ablation.

Methods: From November 2001 to January 2004, 512 consecutive patients underwent surgical treatment for AF at a major Midwest hospital. A prospective computerized database was utilized to collect information on rates of AF recurrence, in-hospital morbidity and mortality, long term survival, freedom from cardiac events, and the prevalence of Coumadin and antiarrhythmic class I/III usage at the time of patient follow-up.

Results: Multivariable analysis suggested that the clinical profile and presentation of AF differs between men and women; women were more likely to have severe valve disease and congestive heart failure while men were more likely to have severe coronary artery disease and history of myocardial infarction. Hence, propensity matching was employed to account for such differences. Unadjusted comparisons showed that rates of AF recurrence ($P=.0005$) and Coumadin usage ($P=.007$) were higher for women than men. However, this difference was not observed in the matched comparisons ($P=.6$, $P=.6$). Matched comparisons did show a difference in the prevalence of antiarrhythmic drugs ($P=.06$), with women appearing to have higher rates especially during the first six months after the procedure.

Conclusions: Our study showed that while gender may be a marker for recurrent AF after surgical ablation, it is in fact not an independent risk factor. However, female gender does appear to be a risk factor for increased use of antiarrhythmic class I/III drugs. These are important factors that clinicians must keep in mind when considering treatment options for patients with AF.

Basic Science/Clinical Research

Hanna Han, MS2

Preceptors:

Benjamin Segal, M.D.

Irah King, Graduate Student

Department of Neurology

University of Rochester Medical Center

Accelerated Myeloid Progenitor Mobilization in a Murine Model of Relapsing-Remitting Multiple Sclerosis

Abstract: Multiple Sclerosis (MS) is a CNS-specific autoimmune disease characterized by demyelination and axonal damage that leads to severe and chronic disability. The current understanding of MS pathogenesis is informed by the animal model Experimental Autoimmune Encephalomyelitis (EAE). Cells of the myeloid lineage such as dendritic cells and macrophages play a critical role in the pathogenesis of EAE. They not only serve as antigen-presenting cells (APCs) for myelin-reactive CD4⁺ T cells during disease induction, but also may act during the effector phase of EAE by directly inflicting myelin and axonal damage within the CNS. Although the lifespan of myeloid cells is brief (1-3 days), they have a dominant presence in EAE lesions throughout the chronic course of the disease. Therefore we question whether the bone marrow provides a continuous supply of CNS-infiltrating myeloid cells during EAE. We used a relapsing-remitting model of EAE to assess changes during the course of disease in: 1) The frequency of circulating myeloid progenitors using methylcellulose-based granulocyte macrophage-colony forming unit (GM-CFU) assays and 2) Bone marrow cell MIP-2 (CXCL2) gene expression using quantitative real-time RT-PCR. We hypothesized that the frequency of peripheral blood GM-CFU would directly correlate with clinical episodes of EAE. Furthermore, MIP-2 mRNA expression, a factor associated with myeloid cell retention in the bone marrow, would be downregulated at times of disease exacerbation.

Results: Our studies show an increase in the frequency of peripheral blood GM-CFU immediately preceding clinical episodes of EAE. Conversely, MIP-2 mRNA expression in the bone marrow is inversely related to periods of accelerated myeloid cell mobilization. Collectively, these data support our hypotheses and suggest a potential role for myeloid progenitors in promoting the pathogenesis of CNS autoimmunity.

Basic Science/Clinical Research

James M. Hildebrand, MS2

Preceptor:

Rollin J. (Terry) Fairbanks, M.D., MS

Assistant Professor

Department of Emergency Medicine

University of Rochester Medical Center

A Survey of Staff Perception of the Role of Clinical Pharmacists in the Emergency Department

Abstract:

Study Objective: Despite the potential impact that emergency pharmacist (EPh) programs could have on medication safety and quality of care in the ED, very few programs exist. This study aims to assess medical and nursing staff perceptions of the value of the EPh programs in terms of their impact on medication safety and quality of care.

Methods: This is a descriptive survey study of a random sample of medical and nursing staff in an academic medical center Emergency Department (ED) with a dedicated EPh program. A 26-item survey instrument was developed using qualitative data to focus on the perceived effect of the EPh and the value of specific EPh functions. Fifty percent of eligible staff were randomly selected and invited to complete a web-based survey. Responses were summarized and confidence intervals calculated. Limitations include generalizability to EDs with different characteristics.

Results: Seventy-five (82%) survey instruments were completed (42 nurses, 33 providers). Ninety-nine percent of all respondents felt the EPh improves quality of care, 96% feel they are an integral part of the team, and 93% had consulted the EPh at least a few times during their last five shifts. Staff felt that the EPh should be available for consults, attend resuscitations, and check orders.

Conclusion: This study finds that doctors and nurses overwhelmingly favor the presence of an emergency pharmacist in the ED, frequently seek their advice, and feel they improve quality of care. The results also reinforce the value of many specific duties of the EPh program.

Basic Science/Clinical Research

Christopher Hogan, MS2

Preceptor:

Mark Noble, Ph.D.

Professor Biomedical Genetics

University of Rochester Medical Center

Effect of Chemical Agents Parthenolide, EGCG, Ciglitazone, Valproate and Sodium Butyrate on Apoptosis of Tumor Stem Cells Isolated from Glioblastoma Multiforme Specimens

Abstract:

Glioblastoma multiforme are the most malignant of brain tumors, with the highest mortality rate and a prognosis of 6-9 months. Glioblastoma multiforme derives its malignancy from the exponential growth of glial stem cells, suggesting that eradicating such pluripotent cells could halt its progression. Our study exposed four lines of human glioblastomas and human neural progenitors to an array of toxic chemicals including parthenolide, EGCG, ciglitazone, valproate, and sodium butyrate. Our goal was to find a cocktail of chemicals that would eradicate the glioblastomas while sparing the human neural progenitors, and perhaps even aiding in their proliferation. Experiments found that most chemicals and combinations of chemicals either destroyed all cells non-specifically or selectively eliminated the human neural progenitors and spared or proliferated the glioblastomas. Chemotherapeutics ideally should eliminate tumor cells and spare or proliferate human progenitors. Thus these results illustrate the unique obstacles in treating glioblastoma multiforme. By using our chemotherapeutic combinations to study the effects on other neoplasms including breast cancer, cervical cancer, and lymphoma this distinction may be further elucidated. Future experiments should be performed to expand upon the knowledge gained from this preliminary study in an attempt to find a chemical combination that produces the desired effects on the glioblastomas. Once this initial goal is achieved, further research should include protein analyses, immunoassays, and oxidative analyses on any promising chemical cocktails or one-drug treatments.

Basic Science/Clinical Research

Julie Hugo, MS2

Preceptor:

Scott McIntosh, Ph.D.

Department of Community and Preventative Medicine

University of Rochester Medical Center

Project FIRM (Family-based Insulin Resistance Management)

A nutritional education program for overweight children, those at risk for being overweight, and their families.

Abstract:

Childhood obesity is a major problem facing the United States, with rates continuing to rise. Childhood obesity is associated with a number of comorbidities including cardiovascular, endocrine, and psychosocial consequences. Risk factors stem from both lifestyle and family based causes. To combat this problem, Project FIRM (Family-based Insulin Resistance Management) began in March 2005. Project F.I.R.M.'s aim is to treat obesity in children, via the family's attitudes and practices. In order, to eliminate some of the environmental causative factors of childhood obesity, the family's lifestyles and habits must be addressed and changed. 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. Two participants and their families completed the five session intervention in the summer of 2006. Participant A's BMI decreased from 44.97 to 44.51, while Participant B's BMI decreased from 31.13 to 29.55. Both sets of participants and their families increased their knowledge and understanding of nutrition and exercise and the impact it has on weight.

Basic Science/Clinical Research

Evan Katzel, MS2

Preceptors:

Richard K. Miller, Ph.D.

Angela Woodall, M.D., Fellow

Department of Obstetrics and Gynecology

University of Rochester Medical Center

Origins of Abnormal Pregnancy: Relationship between Maternal Blood Flow and Placental Outgrowth.

Abstract

Hypothesis: The origins of abnormal pregnancy occur during the first trimester. Abnormal uterine blood flow at the implantation site results in reduced trophoblast cell proliferation and differentiation. These trophoblast alterations provide the basis for the pathological changes that lead to compromised pregnancies, e.g., pregnancy loss, fetal growth restriction and preeclampsia/eclampsia. The goal of this study is to determine the relationship between abnormal maternal blood flow and in vitro trophoblast cell outgrowth.

Methods: Pregnant women between 6 and 9 weeks of gestation, who were terminating their pregnancy for psychosocial reasons, were recruited. To assess uterine blood flow around the implantation site, transvaginal Doppler ultrasonography was performed. In vitro, placental explants were cultured on extracellular matrix (Matrigel) for 7 days. Explants were examined and photographed using an inverted microscope on day 2, and days 4 through 6; media were collected each day to assess extravillous trophoblast growth. On day 6, tissue was fixed, and histological specimens were prepared for confocal imaging using triple stain immunocytochemistry. Cytokeratin 8 (ck-8) for a trophoblast marker, TUNEL and M30 stains were used as an apoptotic marker, and Ki-67 is used to measure cellular proliferation.

Results: Seven pregnancies have been evaluated; in two pregnancies, ultrasound findings demonstrated either a lack of maternal subchorionic peripheral blood flow or increased maternal intravillous blood flow which correlated with poor trophoblast outgrowth in vitro.

Summary: It is anticipated that perhaps 25-30% of early pregnancies will result in pregnancy loss, FGR and preeclampsia. With the current number of subjects, definitive conclusions cannot be drawn; however, the observations to date are consistent with the hypothesis; that abnormal maternal blood surrounding the implantation site during the first trimester is associated with a reduced outgrowth of the trophoblast cells from these early human placentae in vitro. (Supported in part by a Medical Student Summer Fellowship to EK and a grant from the Goode Foundation to RKM).

Basic Science/Clinical Research

Ajay Kuriyan, MS2

Preceptors:

Steven Feldon, M.D., M.B.A.

Chair, University of Rochester Eye Institute University of Rochester Medical Center

Richard Phipps, Ph.D.

Professor, Environmental Medicine, Microbiology & Immunology, Oncology, and Pediatrics

University of Rochester Medical Center

The Correlation between the Phenotype of Orbital Fibroblasts and the Clinical Manifestations of Graves' Ophthalmopathy

Abstract: Graves' disease is an autoimmune disease of the thyroid gland that results in hyperthyroidism. About 50-60% of the patients with Graves' disease develop Graves' Ophthalmopathy (GO), in which orbital fibroblasts are the target of an autoimmune response mediated by T-lymphocytes. Patients with GO are grouped into two categories, Type I, which presents predominantly with enlargement of the orbital fat compartment and little to no enlargement of the extraocular muscles, and Type II, which presents with predominantly enlargement of the extraocular muscles. Type II GO is often associated with more severe symptoms and signs. Interaction between CD40L on T-lymphocytes and the CD40 surface receptor on orbital fibroblasts and other autoimmune pathways cause proliferation, adipogenesis, and a large increase in the production glycosaminoglycans, cytokines, and prostaglandins. This in turn causes a large increase in the volume of orbital fat and muscle, resulting in the symptoms associated with GO.

In vitro examination of the orbital fibroblasts from patients with Graves' Ophthalmopathy demonstrates that some fibroblasts proliferate and differentiate into adipocytes, which is associated with fat enlargement, while others proliferate and produce cytokines and glycosaminoglycans, which is associated with muscle enlargement. This suggests the determinant of the predominance of muscle or orbital fat enlargement is the phenotype of the orbital fibroblast. To test this hypothesis, we will study the clinical manifestations of 31 patients with Graves' Ophthalmopathy and their muscle-to-orbit ratio (cm³) to determine their classification as Type I or Type II patients and correlate that with the in vitro response of the fibroblasts isolated from their surgical orbital biopsy. We will also examine the relationship between the phenotype of affected orbital fibroblasts and the age, sex, smoking behaviors, thyroid status, blood pressure, and cholesterol level of those patients.

Anticipated Results: Although in vitro examination of the orbital fibroblasts are not complete, we anticipate that orbital fibroblasts that favor adipogenesis in vitro will strongly correlate with Type I GO patients and younger patients. We also anticipate orbital fibroblasts that undergo proliferation, secretion of GAG's, and secretion of cytokines in vitro will strongly correlate with Type II GO patients and older patients. Since additional risk factors seem to favor worse manifestations of disease, we also predict that Type II disease and proliferative fibroblast responses in vitro will be associated with female gender, smoking, hypertension, and hypercholesterolemia.

Basic Science/Clinical Research

Judy Liu, MS2

Preceptor:

Arthur J. Moss, M.D.

Heart Research Follow Up Program

University of Rochester Medical Center

Phenotypic Expression of the Congenital Long QT Syndrome in Caucasian and Japanese Patients with Matched KCNQ1 Genotypes

Abstract:

Ethnic differences may affect the phenotypic expression of genetic disorders. The study compared the clinical course of Caucasian and Japanese long QT type-I (LQTI) patients that were matched for mutations in the KCNQ1 gene. The study population comprised 64 Caucasian and 38 Japanese patients enrolled in the International LQTS Registry. The two ethnic groups were matched for six individual KCNQ1 mutations that were categorized into dominant negative and loss of function types. Cox proportional hazards analysis was used to evaluate the independent contribution of ethnicity and mutation type to the occurrence of a first LQTS-related cardiac event (including syncope, aborted cardiac arrest, or sudden cardiac death) from birth through age 40 years.

Results:

Japanese patients with LQTI had a significantly higher cumulative rate of cardiac events than Caucasian patients. The frequency of the high-risk dominant negative mutation-type was 63% and 37% in Japanese and Caucasian patients, respectively ($p < 0.0001$). After multivariate adjustment for gender, QTc, and time-dependent therapy with β -blockers, Japanese ethnicity was associated with a 4.365-fold increase in the risk of cardiac events ($p < 0.0001$). However, when the mutation type was added into the multivariate model, the risk associated with Japanese ethnicity was no longer significant (HR=1.895; $p=0.154$), whereas the dominant negative mutation type was the greatest predictor of risk among study patients (HR=4.66; $p=0.001$). Our data provide evidence that ethnic differences in the clinical expression of LQTS can be attributed to differences in the frequencies of the mutation-type carried by the individual populations.

Basic Science/Clinical Research

Todd Liu, MS2

Preceptor:

Berislav Zlokovic, M.D., Ph.D.

Professor of Neurosurgery and Neurology

Department of Neurosurgery

University of Rochester Medical Center

Activated Protein C Administration Delays Onset and Mortality in a Transgenic Mouse Model of Amyotrophic Lateral Sclerosis

Todd Liu; Zhihui Zhong; Lee Hallagan; Berislav Zlokovic, MD, PhD Frank P Smith Laboratories for Neuroscience and Neurosurgical Research Department of Neurological Surgery and Division of Neurovascular Biology University of Rochester Medical Center

Abstract: Amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's Disease, is a devastating chronic neurodegenerative disease affecting both upper and lower motor neurons often resulting in death. Inflammatory processes in the central nervous system have been observed along with neurodegeneration and are believed to play an aggravating or possibly even a causative role in the pathophysiology of the disease. Activated Protein C (APC) is a protective anti-inflammatory and anti-coagulate therapeutic agent utilized for many other diseases. By administering daily injections of APC [G1], transgenic ALS mice (SOD⁰⁹³ A) demonstrated significantly delayed disease onset ($p < 0.001$) as well as mortality ($p < 0.01$). Markers for inflammation (microglial activation and NFkB upregulation) and motor neuron death (NeuN [G 1]) in the ventral spinal cord were reduced when studied immunohistochemically. APC injections reduced ($p < 0.05$) hemorrhage and blood brain barrier malfunction in the transgenic mice when observed with staining for Prussian Blue and mouse IgG respectively. In conclusion, inflammatory and vascular complications in ALS can be reduced through therapeutic use of APC, which may delay the disease onset and mortality.

Basic Science/Clinical Research

Andrew Marky, MS2

Preceptor:

Berislav Zlokovic, M.D., Ph.D.

Professor of Neurosurgery and Neurology

Department of Neurosurgery

University of Rochester Medical Center

sLRP Administration Increased Brain To Blood Efflux Of Alzheimer's Amyloid-Peptides in 3-Tg AD mice

Abbay Sagare and Rashid Deane

Frank P. Smith Laboratories for Neuroscience and Neurosurgical Research,
Department of Neurosurgery, URMC

LRPI (low density-lipoprotein receptor-related protein) mediated transport of AP40 and 42 from brain have been demonstrated using a brain clearance technique developed in the Zlokovic lab. The extracellular domain of LRPI has four ligand binding domains, I, II, III and IV. A β binds LRP clusters II and IV with high affinity. The purpose of this study was to investigate whether introducing soluble LRP-II (sLRP-II) in mice plasma would sequester A β in plasma and create a gradient for A β efflux from brain. We hypothesized that increased plasma sLRP-II would increase plasma A β levels and reduce brain AP levels. Mice (3-Tg AD) were given either a single bolus (I.V.) of 20 μ g sLRP-II (test) or saline (control) and blood samples collected at pre, and 1, 6, and 12 hrs after the injection. At the end of the experiment, cisternal CSF samples were collected, and brain removed. Hippocampus, cortex and plasma A β 40 and 42 levels were quantified by sandwich ELISA. Lipids (TC, HDL-C) were determined from plasma using kits from Wako Laboratories. Mice treated with sLRP-II showed significantly increased plasma A β 40 and 42 compared with saline treated mice. sLRP-II treated mice showed reduced brain A β 40 and 42 levels, but no change in CSF levels. Treatment of 3-Tg AD mice with a single bolus of sLRP-II showed a significant increase in plasma AP40 and 42, and reduced brain A β while CSF levels were not significantly affected at 12hrs. Lipids (TC and HDL-C) were not significantly affected between these groups. Further studies are needed to confirm these findings.

*Supported by NIH funding to Dr. Zlokovic and OME funding to Andrew Marky

Basic Science/Clinical Research

Emmanuel Menga, MS2

Preceptor:

Regis O'Keefe, M.D., PhD.

Director, Department of Orthopaedics Center for Musculoskeletal Research
University of Rochester Medical Center

TGF-Beta/Smad3 SIGNALING IN MURINE FRACTURE REPAIR AND HEALING PROCESS

Abstract: The endochondral bone formation process in fracture repair and healing involves overlapping metabolic, cellular, vascular and mechanical processes resulting in restoration of the fracture site. The healing sequence include an inflammatory phase involving release of cytokines, angiogenesis and fibroblast infiltration, a repair phase leading to formation of callus and remodeling phase involving restoration of normal structure and function [1]. The regulation of callus transformation in the repair phase involve several growth factors. Transformation growth factor-Beta (TGF-13) plays a major role in the latter process. To investigate the role of TGF-13/sm α 3, a standardized murine femur fracture model is used to examine fracture healing differences between wild type and Sm α 3^{-/-} mice and compare the factors involved in the repair process including, fracture callus mesenchymal tissue, cartilage and bone area. The lack of sm α 3, an effector of TGF-13, leads to a decrease in bone mineral density indicating possible involvement of TGF-13/sm α 3 in fracture repair process.

To investigate the role of sm α 3 in the fracture repair process we completed fractures at various time points (0, 7, 14, and 21 days, n=3). Histology will be used to assess differences in wild type and Sm α 3^{-/-} mice in the areas of mesenchymal, cartilaginous, and bone tissue within the healing callus. Real time RT-PCR using RNA obtained at various time points (0, 7, 14, and 21 days, n=4) will be used to examine the expression of genes involved in cartilage and bone formation. Information gathered from this study could contribute to the framework for developing treatment strategies for improving fracture healing in humans.

Anticipated Results:

It is anticipated that Sm α 3^{-/-} mice will have reduced bone density compared to wild type mice. We expect that the total fracture callus area will be reduced and that sm α 3^{-/-} maturation of cartilage will occur at an accelerated rate. In addition, the histomorphometric findings will permit assessment of the relative amount of mesenchymal tissue, cartilage tissue, and bone tissue present in the callus. We expect that there will also possibly be a delay in the differentiation of mesenchymal stem cells to cartilage tissue. This is a necessary step in fracture healing.

Basic Science/Clinical Research

Kathryn O'Connor, MS2

Preceptor:

Judy Baumhauer M.D.

Director of Foot and Ankle Division of Orthopaedics

Department of Orthopaedics

University of Rochester Medical Center

Outcomes in Posterior Tibial Tendon Dysfunction following Bracing

Abstract: Posterior tibial tendon dysfunction (PTTD) is a common cause of adult acquired flat foot deformity. While classic treatment is surgical intervention, recent studies suggest that non-surgical interventions are also an effective means of treatment in the early stage of disease. At the present time, there are no known variables that can be used to predict the likelihood of success with bracing. Conservative measures are used at initial presentation, with little data describing the progression or resolution of PTTD following these treatments. This study will compare patients who were successful with conservative treatments, over the counter ankle braces, to those patients who required surgery for treatment. In addition patients who were successful in conservative treatment will be contacted to determine what the long term outcomes of bracing were.

Results: At this time data analysis has not been completed. Follow up phone calls are being completed this month. Data will be analyzed once telephone surveys are completed. We expect to submit this paper in the spring of 2007.

Basic Science/Clinical Research

Brock O'Neil, MS2

Preceptor:

Robert Frisina, Ph.D.

Associate Chairman for Research

Professor of Otolaryngology

Department of Otolaryngology

University of Rochester Medical Center

Effectiveness of Insulin for Treating Hearing Loss in Diabetic Mice

Abstract: Type I and Type II Diabetes have been shown to cause a number of metabolic and physiological clinically relevant medical conditions, including hearing loss. For example, we recently reported the nature and extent of peripheral and central hearing loss in aged Type II diabetic human subjects [Frisina et al., *Hear. Res.* 211: 103-113, 2006]. Aggressive treatment of diabetes through medication, exercise and diet, have proven effective for reducing or slowing the progression of various vascular and metabolic diabetic sequelae in many patients. However, no studies have specifically examined interventions aimed at reducing hyperglycemia in order to preserve hearing in diabetic subjects, or slow down progression of hearing loss due to diabetes. The objective of this study was to examine the effectiveness of insulin treatment in preventing or reversing diabetic induced age-related hearing loss in CBA mice. Auditory brain response (ABR) thresholds and distortion-product otoacoustic emission levels (DPOAEs) were recorded in male streptozotocin treated diabetic mice. Preliminary data suggest that by eight weeks after induction of diabetes, all mice showed elevated ABR thresholds at 24 and 32 kHz, and reduced DPOAEs between 35 and 48 kHz. Eight weeks after induction of diabetes, mice were implanted with a subcutaneous insulin or palmitic acid control pellet. Although this portion of the investigation is still in progress, there appear to be differences between mice treated with insulin versus control mice as measured by both ABR thresholds and DPOAEs.

Results: Data collection is still in progress.

Basic Science/Clinical Research

Keith Olsen, MS2

Preceptor:

Terry Wright, Ph.D.

Assistant Professor of Pediatrics and of Microbiology and Immunology

Department of Pediatrics

Strong Children's Research Center

University of Rochester Medical Center

MyD88 Dependent Activation of Type II Alveolar Epithelial Cells by *Pneumocystis Carinii*

Abstract:

Pneumocystis carinii is a pathogenic fungus that causes pneumonia (PCP) in immunocompromised patients, such as those suffering from AIDS or undergoing chemotherapy. Although the exact mechanisms of PCP-related lung injury remain unclear, it is evident that the host's immune response is a major pathogenic determinant. During the course of infection, *P. carinii* attaches directly to alveolar epithelial cells (AECs) triggering an inflammatory response. In vitro, stimulating type II AECs with *P. carinii* results in activation of the NF- κ B and JNK signaling pathways and downstream MCP-1 and MIP-2 production. However, the nature of the *P. carinii*-AEC interaction that leads to this signal transduction cascade remains unknown. The Toll-like receptor (TLR) family of pattern recognition molecules is one potential candidate for initiating the activation of these inflammatory pathways. To determine whether TLRs are involved in the AEC response to *P. carinii*, we utilized primary type II AECs isolated from mice lacking MyD88, a key molecule involved in TLR signaling. As expected, wild type AECs responded to *P. carinii* with JNK activation, MCP-1 mRNA transcription, and MCP-1 and MIP-2 protein secretion. In contrast, MyD88 deficient AECs lack this inflammatory response to *P. carinii* as shown by a decrease in JNK phosphorylation, MCP-1 mRNA transcription, and chemokine production in response to *P. carinii* stimulation. As MyD88 is an important adaptor molecule in the TLR signaling pathway, these data imply that Toll-like receptors are important for the recognition of *P. carinii* by Type II AECs.

Results: Pending

Basic Science/Clinical Research

David Perlmutter, MS2

Preceptor:

Berislav Zlokovic, M.D., Ph.D.

Professor of Neurosurgery and Neurology

Department of Neurosurgery

University of Rochester Medical Center

Normal Aging Increases Copper Levels In Brain Capillaries and Reduces Lrp1-Mediated Alzheimer's Amyloid Beta Clearance from Brain

Deane, Rashid; Sagare, Abhay; Perry, Sheldon; Camprodon, Mireia

Frank P. Smith Laboratories for neuroscience and Neurological Surgery Research, Department of Neurological Surgery and Division of Neurovascular Biology, University of Rochester Medical Center.

Alzheimer's Disease (AD) is marked by deposition of senile plaques containing aggregates of AP bound to metal ions, Zn (II), Cu (II), and Fe (III), and other molecules such as cholesterol and apolipoprotein E. Of these metal ions, Cu binds AP and facilitates its aggregation. The LDL receptor-related protein-1 (LRP1) is the primary receptor for AP clearance across the blood-brain-barrier (BBB) from brain to blood. LRP1 levels in brain endothelial cells (BECs) are downregulated with age, and brain Cu is increased with age. Recently the Zlokovic group has shown a dose-dependent reduction of LRP1 levels and AP42 binding using human brain endothelial cells incubated with 200nM or 2 μ M Cu for 48 hrs. These observations suggest that tracer Cu levels may reduce brain AP clearance across the BBB. To explore this hypothesis further, we measured Cu levels in plasma, brain capillaries and capillary depleted brain by graphite furnace atomic absorption spectrometry, LRP1 levels in brain capillaries and capillary depleted brain by Western blot analysis, and AP levels in brain parenchyma by ELISA in young (1-3 months) and old (21-28 months) mice (C57BL6). Cu concentrations in plasma ($p=.0967$) and capillaries ($p=.0301$) were greater in old mice compared to the young mice. LRP1 expression levels in capillary depleted brain and brain capillaries were lower ($p=.0339$) and AP40 and AP42 concentrations were higher in the older mice compared to the younger counterpart. Therefore, in normal aging Cu levels are increased and LRP1 levels are decreased in brain capillaries. This may reduce AP clearance from brain leading to the accumulation of potentially toxic species in brain. (further work is needed to confirm these preliminary data). Supported by Pilot Project grant to RD, NIH grants to BZ and Schmitt Program on Integrative Brain Research Summer Grant to DP.

Basic Science/Clinical Research

Lars Peterson, MS2

Preceptors:

Manish Shah, MD, MPH, FACEP

Terry Fairbanks, MD, MS, NREMT

Department of Emergency Medicine

University of Rochester Medical Center

Perspectives on Continuing Education in Geriatric Care for EMS Providers

Background: The population of adults aged 65 and older is expanding and uses emergency medical services (EMS) at a high rate. Current estimates find that older adults (age \geq 65) comprise 40% of EMS patients. EMS providers receive very little education in geriatric patient care during their training, particularly considering the size of this population.

Objectives: 1. To identify the primary geriatrics continuing education needs of EMS providers by utilizing key informant interviews. 2. To identify the ideal characteristics of a continuing education program in geriatric care by using key informant interviews from the same population.

Methods: Semi-structured interviews were conducted using an interview guide which addressed the following domains: the current state of geriatric education for emergency medical technicians (EMTs), the current EMT competencies in caring for older adults, recommendations for improvement of continuing education in geriatric care for EMTs, and ideal delivery methods for content. The authors analyzed the data using standard qualitative methods and emerging themes were identified. Demographic information was collected and de-identified so that comments could be considered in the context of the individual providing them.

Participants: The key informants included two geriatricians, two EMS physicians, six EMT instructors and administrators, and ten EMS providers who were not administrators or instructors. All participants provide care in Monroe County, New York.

Results: Prominent themes raised include: the need to improve EMT communication with geriatric patients, provider empathy, addressing the unique issues of polypharmacy in the geriatric population, and improving relationships among different levels and roles of healthcare providers outside the hospital setting. Most individuals feel they are comfortable in assessing a geriatric patient yet there is a need to improve this throughout the EMS system. Additionally, continuing education needs to be offered in various modalities to fit the needs of the learner both in terms of learning process as well as scheduling.

Conclusion: There are several areas of initial education in geriatric care that many of the EMS providers interviewed feel need improvement. Continuing education delivery needs to be tailored to the learner and as such different modalities may need to be developed to include classroom lecture as well as independent learning.

Basic Science/Clinical Research

Bianca Redhead, MS2

Preceptors:

Jeffrey H. Peters, M.D.

Chair of the Department of Surgery

Oliver S. Gellersen, M.D., Fellow

Department of Surgery, Division of Thoracic and Foregut Surgery

University of Rochester Medical Center

Outcomes Analysis of Open vs. Laparoscopic Fundoplication with Type II, III and IV Hiatal Hernias

Abstract:

Paraesophageal Hiatal Hernias (PEH), Type II, III and IV hernias, are very common with a probable incidence of 15%. Many of the hernia patients with paraesophageal hernias who are identified and seek treatment undergo surgical fundoplication to correct the anatomical defect that produces the herniation. Funduplications can be of several varieties, either an open or closed approach, transthoracic or transabdominal. Data on outcomes has suggested a better repair prognosis with the open surgical approach, however, these analyses are often confounded by different study designs and measures. To determine the best surgical approach for Types II, III and IV hernias, follow up data from upper GI studies and self report of study outcome measures regarding symptomology: periop and post operative complications, length of stay, and symptom resolution, are to be gathered from around 60 of the PEH hernia patients who underwent surgical repair from 1997 to 2006. Patients will be chosen randomly from a comprehensive database of all hiatal hernia patients from Strong Memorial Hospital, 1997 to 2006 that was created for this study and future studies. This study is ongoing and results are pending.

Basic Science/Clinical Research

Zachary Reese, MS2

Preceptor:

Robert D. Frisina, Ph.D.

Associate Professor

Otolaryngology Department

University of Rochester Medical Center

Gene Expression Levels of the Potassium Channel Tetramerization Domain: A Possible Association with Age-related Hearing Loss in CBA Mice

Marcus Rampton¹, Mary D'Souza^{1,2} Xiaoxia Zhu^{1,2}

The potassium channel tetramerization domain containing (Kctd) gene family contains an N-terminal sequence homologous to the T1 domain of the Shaker family of voltage-gated potassium channels. However, Kctd proteins lack a transmembrane domain and other aspects of channel proteins. Voltage-gated potassium channels (including the Shaker family) play a critical role in the regulation of the cochlear response to auditory stimuli, and mutations to these channels have been shown to cause hearing loss in mammals. The role of the "Shaker-related" Kctd gene in auditory function has not yet been outlined. The purpose of this study was to determine the relationship between expression of the Kctd gene within the cochlea and age-related hearing loss (presbycusis) in CBA mice. Four groups of mice were defined based upon their age and hearing levels (as determined by ABR thresholds and DPOAE amplitudes): 1) Young controls, 2) Middle-aged with good hearing, 3) Old with mild presbycusis, and 4) Old with severe presbycusis. Microarray RMA normalized data derived from Affymetrix MOE430A GeneChip yielded 105 potassium receptor probe-sets (22 within the potassium channel subset)

Log Signal Ratios (LSR) from the probe-sets were subjected to the following statistical analyses: 1) One-way ANOVA, 2) Linear Regression of LSR vs. ABR or DPOAE, and 3) Fold changes in microarray gene expression. Probe sets with expression changes > 1.2-fold change when compared to young controls and p values < 0.05 were selected for quantitative relative real time PCR confirmation of the expression pattern within aging presbycusis mice. Four Kctd probe-sets (Kctd7, Kctd9, Kctd10, & Kctd12) met the selection criteria, and relative real time PCR validated the microarray results in one (Kctd10) of the four probe-sets.

The results suggest that downregulation of the Kctd10 gene may play an important role in age-related hearing loss in CBA mice.

¹ Otolaryngology Dept., Univ. of Rochester School of Medicine and Dentistry, 601 Elmwood Ave., Rochester, NY, 14642

² International Center For Hearing & Speech Research, Rochester Institute of Technology, 52 Lomb Memorial Dr. Rochester, NY 1462

Basic Science/Clinical Research

Jordan C. Schramm, MS2

Preceptors:

Thanh Dinh, DPM

Surgery, Harvard Medical School Beth Israel Deaconess Medical Center Boston, MA

Aristidis Veves, MD, DSc

Harvard Medical School

Microcirculation Lab and Joslin-Beth Israel Deaconess Foot Center Boston, MA

Microvascular Changes in the Diabetic Foot

Abstract

Impairment of the microcirculation of diabetic patients may contribute to secondary complications in the lower extremity, such as foot infections and ulcerations. These microcirculatory changes, which are mainly functional rather than structural, are responsible for the impaired ability of the microvasculature to vasodilate in response to injury. Dysfunction of vascular endothelial cells and vascular smooth muscle cells both contribute to the reduction in vasodilation that is observed in diabetic patients. Nerve-axon reflex related microvascular vasodilation is also impaired in the diabetic population, and there is a growing belief that both the failure of the vessels to dilate and the impairment of the nerve axon reflex are major causes for impaired wound healing in diabetic patients. Further studies are necessary to clarify the precise etiology of endothelial and smooth muscle dysfunction in diabetic patients so that potential therapeutic interventions may be identified.

Reference:

Schranun JC, Dinh T, Veves A. Microvascular changes in the diabetic foot. *IntJ Low Extrem Wounds*. 2006 Sep;5(3):149-59.

Basic Science/Clinical Research

Valerie Sheppard, MS2

Preceptor:

Anthony Oh, M.D.

Western University of Health Sciences

College of Osteopathic Medicine of the Pacific

Management of the Contralateral Breast in Cases of Invasive Lobular Carcinoma

Invasive lobular carcinoma (ILC) accounts for approximately 10% of breast cancer cases and its appropriate treatment is debated amongst surgeons and medical oncologists. The biologic characteristics of ILC and the desire for a symmetrical outcome from reconstructive surgery may influence a woman's decision to have a contralateral prophylactic mastectomy. The National Cancer Care Network (NCCN), National Cancer Institute (NCI), and Society of Surgical Oncology (SSO) do not currently advocate contralateral prophylactic mastectomy for patients with ILC. While some studies have shown a survival advantage in patients receiving contralateral prophylactic mastectomy for breast cancer, it remains unclear whether this holds true for the subset of patients with ILC alone. Current literature would suggest that contralateral blind breast biopsy is not warranted and that prophylactic contralateral mastectomy is overly aggressive treatment in most cases of ILC. Prophylactic contralateral mastectomy may be considered in selected cases of ILC after appropriate counseling. Emphasis on the selected use of tamoxifen or aromatase inhibitors to prevent contralateral breast cancer in women with lobular primaries, instead of prophylactic mastectomy, may be another reasonable option.

Basic Science/Clinical Research

Deepak Sobti, MSI

Preceptors:

Marilyn Brown, M.D.

Cary Qualia, M.D., Fellow

Department of Pediatric Gastroenterology

University of Rochester Medical Center

Eosinophilic Esophagitis: 30 children's Response to Swallowed Fluticasone

Background: Swallowed fluticasone has become well-accepted as a treatment for eosinophilic esophagitis (EE). A six-week course of therapy is recommended, often in conjunction with dietary modification. Despite improvement in symptoms while taking topical fluticasone, high rates of symptom relapse have been shown upon discontinuation of this medication. The purpose of this retrospective review was to determine the short- and long-term response of children with EE to swallowed fluticasone.

Methods: The charts of 160 children diagnosed with esophagitis (ICD-9 code 530.1x) at the University of Rochester between May 2003 and June 2006 were reviewed. Sixty of these patients were diagnosed with EE by strict histological criteria (≥ 20 eosinophils per high power field). Charts of 30 patients (age range: 1 to 18 years, mean 8.62 years) with EE that had undergone at least two GDs and had been subjected to treatment with swallowed fluticasone were reviewed in greater detail. Sex, age of symptom onset, reported symptoms, specific food allergens, endoscopic findings, number of eosinophils per high power field, the type of intervention (medical and/or dietary), along with the response to the intervention were recorded.

Results: Twenty three (77%) of the 30 patients were male. The most common reported symptoms were dysphagia (53%) and vomiting (50%). Although 29 (97%) of the patients were prescribed a proton pump inhibitor (PPI), only 9 of 22 (32%) were diagnosed with acid reflux during a 24 hour pH probe study off PPI therapy. While taking swallowed fluticasone, 28 patients (93%) experienced a resolution of clinical symptoms, and 29 patients (97%) had histological improvement (decreased number of eosinophils/high power field). Two patients showed no clinical response to swallowed fluticasone. Upon the discontinuation of swallowed fluticasone, 46% of patients sustained a recurrence of their symptoms.

Conclusion: The results of this retrospective study suggest that many patients with EE will ultimately suffer a relapse of symptoms following a six-week course of topical steroid treatment. A longer course of topical steroid may be effective for many, but better therapies need to be developed.

Basic Science/Clinical Research

Cynthia Tung, MS2

Preceptor:

Mina Chung, M.D.

Ophthalmology

University of Rochester Medical Center

Adaptive Optics Imaging in Age-Related Macular Degeneration

Abstract: Because age-related macular degeneration (AMD) is the leading cause of severe vision loss in patients older than 50 years of age in the United States, it is becoming increasingly important to identify patients who are susceptible to AMD at earlier stages in the disease. In the human eye, visual transduction occurs at the retinal photoreceptor cells, and the retinal pigment epithelium (RPE) plays a critical supportive role in the metabolism of photoreceptor outer segments. Clinically and morphologically, inherited macular dystrophies appear to be primary diseases of the RPE, but recent advances in our understanding of the causative genes show that, in certain macular dystrophies, the defective proteins involved in the pathophysiology localize to the photoreceptor outer segments. One potential tool in exploring the cellular mechanism of macular diseases is adaptive optics imaging, a high resolution, non-invasive imaging modality with the capability to examine single cells in the retinas of living patients. We applied *in vivo* adaptive optics imaging of the photoreceptor and RPE cells in patients with genetic mutations known to cause specific macular dystrophies and in descendants of cuticular drusen patients who carry fibulin-5 gene mutations. We hypothesized that on a cellular level, photoreceptor degeneration is the earliest detectable pathologic change in certain macular dystrophies, while accumulation of lipofuscin in the RPE is the first pathologic change in certain other macular dystrophies, an important subset of which is age-related macular degeneration associated with mutations in the fibulin-5 gene.

Results: Results for this experiment are pending.

Basic Science/Clinical Research

Karin Westesson, MS2

Preceptor:

Wael E. A. Saad, M.D.

Assistant Professor of Radiology

Department of Imaging Sciences

Section of Vascular and Interventional Radiology

University of Rochester Medical Center

Inadvertent Discontinuation of percutaneous Nephrostomy Catheters in Adult Native Kidneys: Incidence and Percutaneous Management

Purpose: To evaluate the incidence and consequences of complete inadvertent percutaneous nephrostomy catheter discontinuation in native kidneys of adults. Also, this study evaluated the success rate of nephrostomy tract recanalization.

Materials and Methods: Retrospective analysis was performed in adult patients who underwent percutaneous nephrostomy between January 2000 and December 2005. Patients' conditions were evaluated for complete inadvertent discontinuation and success of subsequent recannulation procedures. Habitual discontinuation was defined by three catheter discontinuation episodes in one patient. Conditions of patients with inadvertent discontinuation were assessed for major complications before and after the recannulation, including the need for de novo nephrostomy to reestablish clinically needed access. The incidences of inadvertent discontinuation and primary assisted recannulation tract maintenance were calculated according to the Kaplan-Meier method. Successful versus unsuccessful recannulation procedures were compared for tract age, length of time the drain was out of the tract and catheter diameter with use of the Mann-Whitney U Test.

Results: A total of 283 patients underwent 325 percutaneous nephrostomies. The inadvertent catheter discontinuation rates at 6, 12, 24 and 36 months were 26%, 26%, 53%, 62%, respectively. For the same time intervals, the primary recannulation assisted tract maintenance rates were 94%, 86%, 77% and 72%, respectively. Habitual discontinuation was seen in 3.2% of the total population and in 19.1% of discontinuation cases. The technical success rates of all and first-time recannulation were 85% and 74%, respectively. Tract maturity was the only variable that was statistically significant between successful and unsuccessful recannulation ($P < 0.0001$). A total of 3.5% of patients required new nephrostomies.

Conclusion: Despite the high incidence of inadvertent discontinuation of nephrostomy catheters, the major complication rate was only 3.5%, indicating the efficacy of tract recannulation, especially in mature tracts.

Community Health Research

Guinevere Casey-Ford, MS2
Lisa Mead, MS2
Sarah Spencer Welsh, MS2

Preceptor:
Christine Wagner, SSJ Director
St. Joseph's Neighborhood Center Rochester, NY

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

Abstract:

The UR Well Student Outreach program is a project of the University of Rochester School of Medicine and Dentistry, working in partnership with St. Joseph's Neighborhood Center to provide free, high-quality preventive and health maintenance services to uninsured and under-served families and individuals. UR Well runs a weekly free primary-care medicine clinic at the Neighborhood Center on Tuesday evenings, offering health care, laboratory testing and a variety of referral and diagnostic services for little or no fee.

This summer, we worked at St. Joseph's Neighborhood Center as training for our Administrative Coordinator positions for UR Well in the 2006-2007 academic year. Our main goals were to build on our strong relationship with the staff at St. Joseph's and to maintain continuity of care during the summer for our Tuesday evening UR Well patients.

UR Well has now been running for 2 years, and our summer project was another step forward for this student-initiated outreach project. We re-organized the appointment schedule for the clinic, double-booking some appointments, and were able to significantly reduce our no-show rate and increase the number of patients we saw each night. We have thoroughly learned the in-house services and the outside referrals that St. Joseph's provides, and we have shared this knowledge with the preceptors and other student volunteers of UR Well. We also updated the database of potential M.D. volunteers for Tuesday nights, making sure that all information was current, and created a phone tree to allow us to rapidly locate an alternate preceptor if our scheduled preceptor were to cancel suddenly.

We continued the smoking cessation program established last summer and streamlined the smoking cessation referrals process, make it easier for providers at St. Joseph's to refer patients to the smoking cessation program, and making it possible for patients to book appointments directly at the front desk. We established a further partnership with the Greater Rochester Area Tobacco Cessation Center (GRATCC), and are now able to offer our smoking cessation program participants free nicotine replacement therapy on-site.

Another goal for the summer was to investigate possible avenues for UR Well to expand its services to another site, allowing us to serve the homeless population to a greater extent than we have at St. Joseph's. We explored several possibilities, including a possible collaboration with the Healthcare for the Homeless project at St. Mary's Hospital. We met with the directors of the program, and have identified several possibilities for student collaboration. These include participation in mass screening and public health programs, health education, and clinical work that might allow us to expand the services or extend the hours offered by the Healthcare for the Homeless. We are currently working with the first-year front-desk volunteers to actively pursue this partnership.

Community Health Research

Danielle Ruppert, MS2
Erinn White, MS2

Preceptor:

Katrina Korfmacher, Ph.D.
Research Assistant Professor and Community Outreach Coordinator
University of Rochester Medical Center
Department of Environmental Medicine

The Healthy Home

Abstract: Rochester's Healthy Home opened its doors to the public in June 2006. The Healthy Home is a residential building set up as a hands-on resource by a partnership of the community groups SWAN, RFRI, and the University of Rochester. The goal of the Healthy Home is to educate members of the community about common, home-based environmental health hazards. Asthma triggers, indoor air pollution, lead poisoning, carbon monoxide, and household chemicals are just a few of the risks addressed in the home. The Healthy Home features guided tours, posters and displays to give residents, property owners, and professionals the resources, knowledge and skills to find and reduce these hazards in their own homes.

Our role in the Healthy Home this summer focused on laying the framework for this project. We created a sustainability notebook to help the Healthy Home run smoothly in the future. We worked to organize a strong core of volunteers, who are responsible for staffing the Healthy Home on an ongoing basis and acting as tour guides. Our other responsibilities included leading tours and facilitating the many events hosted by the Healthy Home. Youth attending SWAN summer camps visited the Healthy Home throughout the summer. We took them on a modified "kid-friendly" tour and helped them complete a puzzle activity to reinforce what they learned in the Home. Many groups, such as Block Clubs, and the Asthma Family Support Group held their meetings in the Healthy in Home. We also helped plan a free Community BBQ held at the Healthy Home at the end of the summer for local residents and families.

Throughout the summer, over 250 people visited the Healthy Home. Visitors to the Healthy Home completed surveys which we collected and entered into a database. This data will allow us to evaluate the helpfulness of the Healthy Home and maximize its effectiveness and accessibility to the community.

International Medicine

Jennifer Abrams, MS2
Brian Jenssen, MS2
Erin Reeve, MS2

Preceptors:
Juan Pena, Ph.D., LMSW
Senior Instructor Department of Psychiatry
University of Rochester Medical Center

Juan Manuel Calvo Rios, M.D.
General Director Sanitario Henri Dunant
Cuernavaca, Mexico

Education, Perceptions, and Practices of Safe Sex in Young Adult Latina Nurses of Cuernavaca, Mexico

Abstract:

In Mexico, increasing rates of HIV/AIDS and unwanted pregnancies are serious public health concerns. Incorrect perceptions of what constitutes safe sex are in part responsible for this upward trend. Therefore, interventions promoting increased contraception education among Mexican young adults have the potential to reduce health risks through behavioral change. We surveyed 60 nurses (Average Age=22.4, SD=4.7) in Cuernavaca, Mexico concerning three aspects of the safe sex practices: where they received education about safe sex, their perceptions of what it means to practice safe sex, and how these perceptions affect their actions regarding birth control and sexually transmitted disease protection. All of the participants received education about pregnancy and STI prevention in school. The majority felt that the sources of sexual education that most influenced their sexual behavior were family and school. At the time of the survey, 69% of participants had sexual intercourse, 42% of which used some method of birth control the first time they had sex. The average age of sexual intercourse was 18.2 years (SD=2.3), with an average number of sexual partners of 1.6 (SD=1).

Although all participants received education about safe sex practices, the survey revealed that subjects were more knowledgeable about birth control than condom efficacy and usage. This is disconcerting considering that the majority of the women use condoms as their primary form of birth control. Also, many women indicated that they consider the rhythm method of birth control at least somewhat effective.

When asked about religion, 95% of women stated that they were Catholic. However, our survey responses showed a deviation from the behaviors and values of what most would consider a traditional Catholic Latin American upbringing. For instance, only 15% of women said that religion influenced their choice to have sex, and only 5% said religion influenced their choice to use contraception. Also contrary to Catholic dogma, only 5% of women said that using birth control was morally wrong. It was assumed that premarital sex would be taboo in this culture; however, many women were comfortable asking their parents about safe sex and 83% reported that they would be able to talk to their parents if they needed contraception. Only 59% of women reported that their parents expected them to remain virgins until they were married.

Part of our concern for the Latino culture was that men were making poor decisions about contraceptive use without consulting their partner. We were encouraged to find that 98% of the women said their partner did not determine whether or not they used contraception. Also, 98% of women felt they would be heard and respected if they asked their partner to stop during sex. This data suggests

that Latina women are actively involved in making decisions regarding sex and birth control.

An important aspect of sexual health to consider is the women's perception of their risk for contracting STIs. According to our survey, 50% of women believe that they are at high risk for acquiring HIV, and 90% said that they would suffer greatly if they contracted HIV. This suggests that they are highly aware of HIV in their society and have been educated enough about HIV to fear its consequences. A culturally relevant finding from our survey was that while 90% would suffer from HIV, only 12% said that they would suffer greatly if they became pregnant. This reflects a large cultural difference in perspectives on pregnancy, and implies that fear of STIs is stronger than fear of pregnancy, possibly motivating them to use protection.

Lastly, when looking at the reported practices of the women who took our survey, 90-95% of the women responded that they did not think it was a big hassle to prevent pregnancy and STIs, although 30% said it was too difficult to have contraceptives available during intercourse. When asked about obtaining contraceptives, 87% said it was easy for them to obtain birth control.

Our survey informed us about the effectiveness of sex education in traditional societies. We need to keep in mind, however, that our subject population of nurses gives us data that is not necessarily applicable to the general population. We assume that those who work in the health care industry will have greater access to both accurate information and a place to obtain proper contraception.

International Medicine

Nadia Awad, MS2

Preceptors:

Mohamed Hassan, M.D.

Professor of Obstetrics and Gynecology

Director of the Labor and Delivery Unit

Ain Shams University, Cairo, Egypt

Department of Obstetrics and Gynecology

Barbara Davis, Ph.D.

Department of Neurobiology and Anatomy

University of Rochester Medical Center

Motivations for Egyptian Women to Seek Infertility Treatment: Implications for Delivery of Treatment and Services

Abstract:

In Western society, infertility is considered a condition with relatively few social repercussions and can be circumvented easily by adoption or by the use of artificial reproductive technologies and techniques. However, infertility presents major social, cultural, and financial issues in developing countries, especially those with ideologically pronatalist societies, such as Egypt. Childlessness is particularly sensitive in the Middle East because both childbirth and rearing are considered family commitments and are inherently related to a woman's social status.

Studies have been performed to assess the causes of infertility in Egyptian women, and while most of these studies infer general reasons Egyptian women seek infertility treatment, none explicitly survey the women to discern specific motivations for seeking treatment. In this study, 45 Egyptian women seeking infertility treatment at the Ain Shams University Hospital were surveyed to determine the major factors influencing their decision to get treatment and how this information could impact the delivery of treatment and services available.

Results:

In the group of women studied, only a quarter have children and only about half have ever been pregnant. The longer a woman has been seeking treatment is inversely correlated with the probability of having a child or ever having been pregnant. The reasons for coming to the office are few, including for an examination or consultation (34%), follow-up treatment (31%), a desire to become pregnant (22%), or a procedure (13%). The women who have been receiving care longer almost exclusively come to the office for a procedure or follow-up treatment (75%). While personal desire to become pregnant is a large factor in seeking treatment (24%), pressure from her husband or family (18%) or the feeling that pregnancy is an expectation of life for a family (38%) outweigh personal decisions.

Regardless of how long a woman seeks treatment, a doctor's influence to go to the clinic remains constant, with about a third of all women coming into the clinic on the advice of an MD. While the influence and advice of relatives is very important in persuading a woman to come into the clinic for the first time, the weight of their input decreases over time. Sixty percent of all women coming to a clinic for the first time are influenced by relatives, in contrast with only 12.5% of repeat patients in the clinic claiming to have been influenced by relatives to come. A woman's office choice is largely based on reputation of the clinic or doctors at the clinic (36%).

However, once a woman chooses a clinic, she tends not to know what to expect at the clinic nor

does she have an opinion of how her treatment should progress. Most of the women (60%) studied have an infertility diagnosis, with the most common diagnosis being anovulation due to polycystic ovary (37%), and most of the women have received hormonal therapy (71%). The women tend to know only of only treatments they have received and they only know of those treatments through their doctor.

In order to better serve the women, more information about infertility treatment and what to expect at the clinic upon arrival could help better deliver infertility treatment. Because pregnancy and child-bearing is considered a defining part of a woman's life, emotional support and guidance could help ease the process of obtaining treatment. Also, education about their condition and options for treatment could help women become more involved in their care.

International Medicine

Jonathan Black, MS2

Preceptor:

Timothy Dye, Ph.D.

Associate Professor

Department of Community and Preventative Medicine

University of Rochester Medical Center

Sasikala Nataraj

An Assessment of Water Use and Sanitation Behavior in Rural Tamil Nadu, India

Objectives: This study examined the relationship between water sources, water usage, water storage, toilet practices, and the incidence of diarrhea in two villages in Tamil Nadu, India.

Background: Poor hygienic practices are utilized in India during water collection and storage, there is limited access to toilet facilities, defecation directly into the water supply, and a lack of water purification, filtration, and boiling prior to consumption. **METHODS:** Surveys were implemented and accompanied by discussion shaped by open-ended questions. **RESULTS:** In total, 96 households were surveyed: 39 households in Edyan Chevadi and 57 households in Kottakari. Of the households surveyed, 99.1% regularly used municipality water. 58.6% believed municipality or bore well water was good quality and 6.6% believed that "all water" was good quality. 99.1% stored their water in open-air buckets. 19.6% regularly boiled or filtered their water prior to consumption. In addition, 1.3% of households boiled water before consumption by children, 13.4% boiled their water after it rained, and 14.6% boiled their water when a member of the household was sick. 25.8% had *at least* one family member experience more than 10 episodes (5+ consecutive loose stools) of diarrhea over the previous year while 9.9% more experienced between 8 and 10 episodes. 78.2% didn't know what caused diarrhea and 87.9% used the outdoors as their toilet.

Conclusions: Based on the high incidence of diarrhea, the toilet practices of villagers, and water storage and usage practices, there is insufficient knowledge in these villages regarding water-borne illnesses and their transmission.

International Medicine

Sean Brady, MS2
Kimberly Lai, MS2

Preceptors:
Ann Dozier, R.N., Ph.D.
Assistant Professor
University of Rochester Medical Center
Department of Community and Preventive Medicine

Herbarth Torres, M.D.
Regional Director of the Seguro Social
Hospital JESS

Factors Affecting the Diets of the People of Cacha, Ecuador

Abstract:

There is a lack of qualitative research describing the factors that affect diet in developing countries. A generally accepted link exists between diet and chronic diseases such as osteoporosis, anemia, diabetes and cardiovascular diseases. Because a variety of factors affects what one eats, this study seeks to understand the hypothesized relationship between food choices and influences of cultural, social, political, and economic origin in Cacha, Ecuador. Data was collected through a series of 20 interviews of patients and community members conducted at the Cacha Subcentro de Salud and the surrounding area. The interviews revealed that the most common motivation for purchasing certain foods was affordability. Although many of the participants stated they ate a larger quantity and a higher quality of food than they ate as children, only five of the twenty participants consumed dairy products and only ten of the twenty ate meat on a regular basis. The majority of participants never received, or could not recall, specific nutritional information. The results suggest that a major obstacle for the Cachan people in buying healthy food is the lack of finances. It is hopeful that improvement in the education of adults and children can help the Cachan people to use the limited resources that are available to make healthier food choices.

International Medicine

Youngsun Cho, MS2

Preceptors:

Eric Caine, M.D.

Professor of Psychiatry

University of Rochester School of Medicine

Bong-Jin Hahm, M.D.

Psychiatry

Seoul National University School of Medicine

Assistant: Molly Jung

Perceptions of and Motivations for Suicide Among Korean College Students

Abstract:

In 2004, the Organization for Economic Cooperation and Development (OECD) released statistics that ranked Korea first in terms of the rate of increase in suicides; during that same year, suicide was the leading cause of death among Korean people in their twenties and thirties-yet, South Korea and other Asian countries are known to stigmatize suicide, highlighting an interesting paradox, and suggesting further exploration into cultural values. A dual-layer exploratory study consisting of in-depth interviews with Korean students (from the general population and from an ideator population) at Seoul National University, and an archive search of the widely-read newspaper *JoongAng Ilbo*, was done in order to begin to understand the perceptions of and possible motivations for suicide among Korean college students. Analysis of these two layers suggests that suicide is viewed as a multi-deterministic event, with the following features: 1. suicide is viewed by Korean culture as a weak act that expresses a lack of courage; 2. depression and difficult situations are thought to be strong contributors to the decision to suicide; 3. specifically, academics, and the closely related topic of future economic prospects, are thought to be great stressors in the lives of SNU students, and potential contributing factors towards suicide consideration. These results are best understood in the context of Korean cultural influences-specifically Buddhism and Confucianism-as well as modern Korean society and the life of a typical Korean student. In addition, these results suggest that treatment approaches for suicidal ideation should include both pharmacologic treatment, and therapy designed to help patients deal with environmental stressors. These results, as well as the exploratory nature of this study, prompt further research into this topic, ideally with a more diverse population, and with the overall objective being to understand perceptions and motivations for suicide in Korean culture thoroughly enough to suggest relevant treatments and interventions.

Results: Pending

Interviews:

Students felt that Korean culture was "Hardly Accepting" of suicide, and responded that society views suicide as a weak act that expresses a lack of courage. When given a question with multiple contributing factors of suicide, and asked to rank the top three, students consistently ranked depression as the primary contributing factor. However, during open-ended discussions prior to the presentation of that question, every student spoke of suicide as the result of a difficult situation, specifically the uncertainty of academics and subsequent employment – depression was rarely mentioned. Academics, and the closely related topic of future economic prospects, were thought to be

great stressors in the lives of SNU students, and potential contributing factors towards suicide consideration.

Newspaper Search:

362 articles on suicide were published between June 2005 and June 2006 in *JoongAng Ilbo-an* average of twenty-eight (+/- 5) articles each month. 89% of the articles had the word suicide (*ja-sal*) in the headline; six of every seven articles were either a Case Report (CR) or a Special Account (SA). 65% of these articles were categorized as CR; SA articles constituted 23%. Attempts constituted 16% of total articles published.

Among the CR and SA articles, 79% reported a reason for the suicide. Of these, three out of every four articles attributed the suicide(s) to a social reason, and one of every four articles attributed the suicide to a mental health problem. 29% of the suicide accounts featured high suicidal detail. 94% of the articles reported the method of the suicide, and 31% of these articles depicted the methods with highly detailed information.

International Medicine

Ravi DeSilva, MS3

Preceptor:

Nancy, Chin, Ph.D., MPH

Assistant Professor

Division of Public Health Practice, Community & Preventive Medicine

University of Rochester Medical Center

Healthcare Assessment on the Tibetan Plateau: An Initial Medical and Anthropological Evaluation of Cardio Vascular Disease Rima Village, Qinghia Province, People's Republic of China

Abstract:

In an effort to assess the healthcare needs of Rima Village, Qinghia Province, People's Republic of China and facilitate proper resource acquisition for the new medical clinic currently under construction several basic health screening programs were conducted during July 2006. These included blood pressure screening as well as assessment of local diet and social factors such as smoking status and alcohol consumption.

To accomplish these assessments the group worked with the four communities that make up Rima Village, as well as Ayan Monastery and the Ani Gumpa (a local convent) through focused interviews and screening programs. Thus this research constitutes an initial medical and anthropological evaluation of local needs upon which additional and more complex research, intervention, and village based cooperation may be undertaken.

Results:

Sixty-three blood pressure measurements were obtained before a mercury leak in the blood pressure cuff led to a suspension of the screening process.

In the course of measuring blood pressure the group was intrigued at the relative lack of hypertension in the community considering observations of diet (specifically high salt consumption), nutrition (high intake of animal fat with few fruits or vegetables), and environmental exposure (increasing community reports of tobacco and alcohol consumption as well as increased dependence on motorized transportation).

The reasons for this low incidence in high blood pressure could be numerous and may be explained by a series of important limitations including incorrect perception of daily diet including sodium intake, an unknown total daily calorie intake, as well as incomplete understanding of exercise/exertion patterns. Genetic factors may also have a significant contribution to the recorded observations.

It is also clear that the age stratification is significantly skewed towards younger persons and many more villagers must be evaluated. Additionally, smoking status and alcohol intake status were very low in the population studied and it is unknown what the true prevalence of these exposures may be in the larger Rima Village population.

Many of those evaluated were from families that included local village leaders and this social status may also reflect a difference in access to resources and/or education which may also skew the data collected

While the team was in the field an important incident occurred that may directly impact the continued evaluation of this community health problem. A 27 year old Ani (nun) who was described as "fine in the morning" subsequently suffered a massive headache and subsequently died. A local

village doctor (one of four in the community) assessed the cause of death as being a cerebral aneurysm. No autopsy was performed.

According to local custom the nun was to be given a sky burial which consists of dismembering the body and allowing birds of prey to consume the flesh. Selected monks have the responsibility to prepare the body for this burial process and it was inquired as to whether or not they observed unusual amounts of blood around the brain at time of dismemberment. No information was available to make an assessment.

Nonetheless, if cerebral aneurysm is the disease process that is responsible for the severe headaches and subsequent morbidity and mortality in the community a very different approach and intervention plan may be necessary than interventions intended to manage and treat hypertension and atherosclerotic disease.

International Medicine

Shahla Jilani, MS2

Preceptors:

Nancy Chin, Ph.D., MPH

Department of Community and Preventative Medicine

University of Rochester Medical Center

Esteban Avendano-Fernandez, M.D., MPH

Director a.i., Costa Rican National Cancer Institute

Carmen Di Mare Hering, MD, MPH

Perspectives on the Use of Complementary Medicine: A Qualitative Examination of Patients, Physicians and Healers in San Jose, Costa Rica

Abstract: With a spectrum of practices ranging from herbal therapy to chiropractics to healing folk rituals, one of the key distinguishing features of complementary medicine has been its unique approach toward holistic patient care. While the practice of complementary medicine has grown significantly in many western countries, including the U.S., it has been a historical mainstay of most Latin American countries, particularly, Costa Rica. Presently, Costa Rica represents a unique intersection of both westernized medical practices, and traditional views of folk medicine. Therefore, we aimed to examine the attitudes and perspectives of Costa Rican patients, physicians and healers toward the use of complementary medicine. Subjects from distinct socio-economic and medical backgrounds were recruited for focused interviews centered on 1) their motivations for practicing complementary medicine, and 2) the effects of such practices on health and wellness. Qualitative analysis following an inductive format revealed a number of recurring and convergent themes. Firstly, in contrast to the U.S. where most users of complementary medicine are higher-educated and affluent females, a more diverse cross-section of Costa Ricans practiced this form of medical therapy. Costa Ricans of both higher and lower socio-economic classes living in San Jose tended to employ the widespread practices of complementary medicine available in their country- which included sobador, homeopathic and herbal healing. Secondly, the majority of Costa Ricans interviewed preferentially incorporated the use of complementary medicine into their daily health practices. The efficacy of long-term complementary medical therapy was a widely held perspective among Costa Ricans living in San Jose. Thirdly, the majority of subjects interviewed limited the use of conventional westernized medicine to only those situations when emergency medical attention was necessary, reverting to complementary medicine for both long-term and preventative health care.

International Medicine

Aunali Khaku, MS2

Preceptors:

Laurence Guttmacher, M.D.

Department of Psychiatry

Nancy Chin, PhD, MPH

Department of Community and Preventative Medicine

University of Rochester Medical Center

Dr. Norah Hogan (Tanzania)

Muhimbili University College of Health Sciences

Department of Psychiatry

Psychiatric Illness and Stigma in Tanzania: A Qualitative Study

Abstract:

Introduction: Considerable research supports the view that mental illness is accompanied by a greater degree of social stigma than somatic illness. Research has also shown that stigma harms patients and is deleterious to society as a whole. Since neither healthcare providers nor patients themselves are immune from the effects of stigma, the best way to alleviate if not eliminate its deleterious effects is to understand it in order to then design programs to counter it. While stigma associated with mental illness has been extensively studied and documented in the West, not much has been done in the rest of the world. Since culture plays a great role in this phenomenon, it would be unwise to superimpose the current Western models in non-Western settings. Hence this study sought to understand the sociological frameworks that underlie stigma towards the mentally ill in Tanzania.

Methods: Qualitative interviews regarding mental illness were conducted using four subject groups: patients, relatives, unrelated non-patients, and healthcare providers. Five representatives from each group were initially interviewed. Later more subjects were added in certain groups to achieve saturation. In order to provide a more comprehensive understanding of the views of the subject, open-ended interviews were used rather than a formal questionnaire. Although the format of the interview was non-structured, demographic data (age, gender, and religious affiliation) were collected at the beginning of the interview. The interview was recorded on a digital recorder.

The interviews were translated and transcribed and the data generated was tabulated using an Excel spreadsheet. The spreadsheet and the transcripts were preliminarily analyzed to find common themes which are reported below. This data will be further refined by coding using 3 independent investigators.

Results: In a preliminary cut of the data, the analytic team was able to identify 9 inter-related themes regarding mental health and stigma in this study population:

Theme 1: Multifactorial etiology

Theme 2: The perception that the general public does not understand that mental illness has a multifactorial etiology and thinks instead that evil spirits/demons/jinn are the causative factors

Theme 3: Mental illness as a correlate of drug/alcohol abuse, with an increased prevalence of disorders

among youth, coupled with the perception that both drug abuse and the incidence of mental illness are on the rise in Tanzania

Theme 4: Fear of the mentally ill as potentially aggressive and dangerous

Theme 5: Mentally ill persons as permanently disabled by their condition due to the chronic nature of the disease and the propensity for frequent relapses leading to 1. the patient not being allowed to do anything productive after the diagnosis and instead being ignored, neglected, and viewed as unable to contribute to society. 2. Considering the mentally ill patient as a burden and a strain on resources.

Theme 6: Labeling of the patient, leading to every subsequent action being judged by the label

Theme 7: Teasing, calling names, and subjecting the mentally ill to humiliation as a source of entertainment

Theme 8: Relatives hiding the diagnosis from others, and hiding the patient from the public

Theme 9: Too many mentally ill; too few resources to cope with the same

Conclusion: The study found a wide variety views, some stigmatizing, and some not, regarding mental illness in Tanzania. Further analysis of the stigmatizing views will go a long way in providing efficient care for the mentally ill and in designing programs to alleviate stigma against the mentally ill in Tanzania.

International Medicine

Cathy Lee, MS2
Rebecca Ryan, MS2

Preceptors:
Mark Shelly, M.D.
Department of Family Medicine
University of Rochester Medical Center

Dr. Mamadou CISSE
Director
CESAC (Centre d'Ecoute, de Soins, d'Animation et de Conseils)
Bamako, Mali

Incidence of Stavudine-Related Peripheral Neuropathy in HIV-Positive Patients in Bamako, Mali

The government of Mali, with financial support from the Global Fund, has dedicated itself to addressing the pandemic of HIV/AIDS within the country. Towards this end, the government has developed an anti-retroviral treatment regimen composed of Nevirapine (ddI), Stavudine (d4T) and Lamivudine. The goal of the program is to have 80% of HIV-infected people in Mali on this specific tri-therapy. These medications were selected for various reasons, including financial viability, availability and efficacy. One of the most common side effects of treatment with Stavudine is peripheral neuropathy, with published rates of peripheral neuropathy varying between 8-36%.

Physicians in Bamako working with HIV/AIDS patients have anecdotally noted a high frequency of patients presenting with peripheral neuropathy. This retrospective study further explores rates of peripheral neuropathy amongst people with HIV/AIDS being treated with Stavudine. This was accomplished by analyzing 362 medical charts of patients who started treatment with Stavudine between January 1, 2005 and June 30, 2005. We looked for the reported incidence of peripheral neuropathy during the first year of follow-up.

Of the 362 patient charts that we reviewed, 29% were lost to follow-up during the year after the beginning of ART and many more had significant lapses in treatment. Furthermore, several patients experienced HIV/AIDS-related peripheral neuropathy prior to beginning ART and were therefore excluded from the study. As a result, we were able to use 178 charts for our data analysis. Of these patients, 58 (33%) experienced symptoms of peripheral neuropathy during the first year of follow-up. Peripheral neuropathy was not related to sex, age, hematocrit nor weight (the primary determinant of dosage). However, incidence of neuropathy could be related to average CD4 count at the beginning of ART. Additionally, onset of neuropathy peaked during the fourth and fifth months of treatment.

Because tri-therapy including Stavudine is so common as first-line HIV/AIDS treatment in developing countries, appropriate protocols need to be put in place to address these high rates of peripheral neuropathy. Furthermore, perhaps the first-line treatment options for HIV/AIDS need to be reconsidered due to these high rates of peripheral neuropathy.

International Medicine

Elizabeth Loomis, MS2

Preceptors:

Michael Keefer, M.D.

Department of Infections Disease

University of Rochester Medical Center

Esper Kallas, M.D.

Sao Paulo, Brazil

Behavioral Risk Factors for Syphilis and Hepatitis Band C in HIV- Infected Adults in Sao Paulo, Brazil

Abstract:

Objective: With over 38 million people infected, HIV continues to be a global problem. Since HIV shares many risk factors with other sexually transmitted infections such as syphilis and viral hepatitis (B and C), persons already infected with HIV may also be at a higher risk for those diseases. Co-infection with HIV and syphilis or with viral hepatitis can create a positive synergy in which the disease course and prognosis for either disease is worsened. We therefore set out to identify which risk behaviors for syphilis and viral hepatitis are most prevalent in an HIV positive cohort in Sao Paulo Brazil, and whether or not engagement in these behaviors has increased since diagnosis with HIV. We hope to use this data to better design co-infection prevention programs.

METHODS: We conducted surveys with 42 recently HIV-infected patients during their normal once every three month clinic visit (F/M=5/37; mean age=33.2 years, range 22- 56; mean time from diagnosis with HIV= 24.1 mo, range 1-49). We also compared current survey responses with answers given to similar questions on risk behaviors at the initial time of HIV diagnosis of the patients.

RESULTS: We found patients engaged in an average of 2.5 risk behaviors out of the 17 that we asked about (range 0-6). Of those behaviors, 33.3% of patients had sex with HIV positive persons, 31.0% reported inconsistent condom use, and 40.5% had three or more sex partners in the last six months. There was a small and insignificant increase in risk behavior from the four months before HIV diagnosis to the 6 months before the survey (Aug, 2006) from 1.05 behaviors out of seven asked about to 1.26. **CONCLUSION:** In our group of HIV positive patients, there is a serious risk of contracting either syphilis or viral hepatitis. The behaviors that put these patients most at risk centered around unsafe sexual practices (poor condom use and multiple, risky partners). While risk behaviors may not have significantly increased since diagnosis with HIV, we should be trying to decrease them by education programs that focus on constant condom use with all partners and for all sexual activities.

International Medicine

Elise Meoli, MS2

Preceptor:

Stephen Lurie, M.D.

Assistant Professor

University of Rochester Medical Center

Department of Family Medicine

Herbarth Torres, M.D.

Professor and Director of Post Graduate Training Hospital I.E.S.S.

Riobamba, Ecuador

The Use of Indigenous Medicine and Its Effect on Health Care Behavior in the Rural Andes of Ecuador: Striking a Balance between Indigenous Medicine and Western Biomedicine

Abstract:

The use of indigenous medicine as a source of primary health-care is widespread in developing countries. For many rural communities indigenous medicine offers a system of health-care that is more accessible and affordable, effective psychologically and in some cases physiologically, and more aligned with their world view and beliefs. This study investigated the health-care seeking behavior of the people of Riobamba, Ecuador. Patients attending Cacha Subcentro de Salud, an indigenous health-care facility, and Hospital Andino, a traditional medicine clinic, were recruited to participate in a survey aimed at garnering information about their health behavior and beliefs as they relate to indigenous and Western medicine. In addition, health professionals from both clinical settings were interviewed to elucidate their perception of the interplay between biomedicine and Andino medicine usage.

Results:

The interviews revealed several themes, some of which were consistent among the patients at both Cacha Subcentro de Salud and Hospital Andino, and some of which were specific to one site or the other. Patients at both sites who believed in the usefulness of Shamanism stated that they chose to use Andino medicine in part because it takes into account the spiritual and psychological aspects of health better than biomedicine. Several patients at Hospital Andino also reported utilizing Andino medicine for treatment of issues that the biomedical system in Ecuador had been unable to resolve. In Cacha, age and level of education were important factors in whether or not a person believed in the value of Andino medicine practices that require a Shaman, whereas the use of medicinal plants was nearly universal.

International Medicine

Jennifer Riehl, MS2
Jessica Rosenthal, MS2

Preceptors:
Noelle Andrus, Ph.D.
Assistant Professor
University of Rochester School of Nursing
Community Health Promotion Education

Vincent Duron, MS4

A Study Examining Antenatal and Perinatal Care in a Malawian Village: An Assessment of Knowledge Base, Access to Resources, and Health Outcomes

Background: The results of a pilot study conducted in the summer of 2005 examining the needs of a community in Malawi, Africa demonstrated the need for education and behavior change surrounding issues of nutrition, sexual health, and disease prevention. The most salient needs addressed were those of better access to information taught in the current antenatal care classes and improved teaching methods for these classes.

Objective: The overall aim of this study was to gain a better understanding of perinatal care and education. Specifically, this study examined current antenatal and perinatal care practices and knowledge among healthcare providers in the community, as well as current antenatal care class curriculum content. In addition, this study examined the demographics of the women attending the antenatal care practices.

Methods: We conducted semi-structured interviews with all seven clinic perinatal healthcare workers of varying titles, including midwives, Health Surveillance Assistants, ward attendants and clinic administrators. We observed three antenatal care classes and a number of deliveries and compared the content of classes and birth practices to World Health Organization (WHO) guidelines for effective newborn interventions in developing countries. Additionally, we interviewed all 89 attendees of three antenatal care classes. **RESULTS:** We analyzed the division of responsibilities among perinatal care providers, identifying a division between midwives as birth attendants and all other workers as educators. Clinic workers identified lack of adequate resources and medical supplies as major barriers to care. Observations of antenatal care classes revealed that only 52% of suggested antenatal care guidelines were included in the current curriculum. Analysis of antenatal care class demographics showed that the mean age of women attending the antenatal care classes was 24 years, with a mean highest level of education of six years. Mean number of pregnancies was three per woman, with a mean gestational age of 21 weeks at first class attendance.

Conclusions: We determined that a major barrier to effective provision of services was lack of standardization and communication among staff members. One effective intervention would be to assist with a revamping and formalization of the antenatal care curriculum, including expansion of topics and use of more interactive teaching techniques. Additionally, a plan should be created to recruit women into antenatal care classes earlier in their pregnancies. Once these interventions have been put into place, assessments should be made of class attendees' antenatal care knowledge.

International Medicine

Otto Thomas, MS2

Preceptors:

Michael Keefer, M.D.

Department of Infectious Disease

University of Rochester Medical Center

Esper Kallas, M.D., Ph.D.

Paulista School of Medicine

Federal University of Sao Paulo - Sao Paulo, Brazil

Potential Direct Effect Between CCR5-Downregulating HIV Infection Inhibitors: Does GBV-C Regulate GATA-1 and GATA-3?

Abstract

Introduction: A variety of biochemical factors have been identified that show protective effects against HIV in human T lymphocytes. These factors range from simple proteins to viruses. One pair of such proteins, GATA-1 and GATA-3, and one virus, GBV-C, have independently been shown to exhibit HIV inhibitory effects through pathways that intersect at common down-regulation of the helper T-cell membrane receptor CCR5. This project ultimately seeks to characterize the cumulative protective effect, whether additive, co-inhibitory, or potentiative, of these factors on human T lymphocytes indirectly- through examining whether GBV-C, its own infective mechanism independent of CCR5, directly regulates transcription of GATA-1 and GATA-3 RNAs. Instrumental to this project is identifying which patients within the assembled laboratory cohort are GBV-C positive and actively express GBV-C proteins, then developing an optimal protocol for promoting transcription of GATA-1 and GATA-3 in normal T lymphocytes so that it may ultimately be applied to GBV-C infected cells.

Methods: Plasma was isolated via centrifugation from HIV (-) donors during peripheral blood mononuclear cell (PBMC) separation. Total donor RNA was extracted from this plasma, cDNA produced, and PCR used to generate DNA sufficient for evaluation of viremia via gel electrophoresis using a GBV-C probe. After verifying GBV-C viremia in 15 patients through repeating the above steps for positive samples, a schematic protocol for GATA-1 and GATA-3 transcription was constructed.

Results

Of the 57 patients evaluated for GBV-C plasma viremia, 15 were found positive, suggesting an infection rate of 26% among HIV (-) controls in this cohort. The protocol constructed for GATA-1 and GATA-3 stimulation utilizes varying concentrations of three stimuli applied independently: IL-2, CD3/CD28, and PHA.

International Medicine

Lauren Ullman, MS2

Preceptor:

Chin-To Fong, M.D.

Department of Pediatrics and Genetics

University of Rochester Medical Center

Abstract:

Infant mortality is a significant problem in the rural areas of China. One of the factors that may contribute to the problem is the lack of prenatal care administered in these areas. A team of investigators from the University of Rochester in Rochester, New York, visited Rima Village, Qinghai Province, China, for three weeks to assess the villagers' knowledge of prenatal care. An IRE-approved study was administered to five women in the village addressing socioeconomic status, nutrition, prenatal care received, environmental exposures, chronic and acute diseases contracted before pregnancy, and a family history of premature birth. The limited results provide an interesting glimpse to the multifaceted issues that can impact the outcome of pregnancy. However, in order to further the study, a number of logistic, cultural, political and economic problems will need to be addressed. Some of these challenges, as well as proposed solutions, will be discussed.

Results:

Five women were interviewed in this study. None of the women interviewed received prenatal care. They did not take folate or have ultrasound screenings during the pregnancy. One woman had an ultrasound because of complications due to the pregnancy. She visited the county hospital for her care. No other women visited a hospital. Very few women in the community consult a doctor at all when pregnant. All women consult a lama, rimpoche, or other religious figure during the pregnancy. Each woman reported praying and chanting with the lama, and making religious offerings to religious figures to help ensure an uncomplicated delivery. Diets of all five women during pregnancy consisted of few fruits and vegetables, and a high quantity of yak meat, yak yogurt, butter tea, soda and candy. Four women were illiterate, and had received no education. One woman had received minimal education, and could read and write. All of the women's husbands were yak herders. Throughout their pregnancies, all women continued to participate in their daily activities, which involved hard labor. They cooked, collected and dried yak dung, churned yak butter and yak yogurt, milked yaks, made yak-hair thread, fetched water, fed dogs, and roasted and ground tsampa. None of the women or their husbands had a family history of premature birth.

Discussion:

There were many challenges to acquiring high-quality study data, including a lack of adequate transportation, limited communication between villages, language barriers, and cultural taboos. These barriers must be overcome in order to provide education about prenatal care to the village doctors and the members of the community. Moreover, understanding the overall health care delivery system beyond the village level, including at the county, prefecture, province and national level will be very helpful. In order to accomplish this goal, it is proposed that an interdisciplinary group involving western physicians, local physicians, translators, and religious and community leaders receive extensive, long-term training at the village site.

International Medicine

Alexis Weymann, MS2

Preceptor:

Nancy, Chin, Ph.D., MPH Assistant Professor
Division of Public Health Practice, Community & Preventive Medicine
University of Rochester Medical Center

Birthing Kits in Tibet

Abstract:

In an effort to assess the healthcare needs of Rima Village, Qinghai Province, People's Republic of China, and facilitate proper resource acquisition for the new medical clinic currently under construction, several basic health screening programs were conducted during July 2006, including Birthing Kit (BK) distribution and assessment of use and effectiveness of previously distributed BKs, prenatal care and maternal nutrition investigation, and blood pressure screening. The Birthing Kit project was initiated particularly in response to local concerns that the incidence of maternal death during deliveries was increasing. By providing hygienic conditions, BKs have been shown to decrease the risk of post-partum infection in mother and newborn, thus lessening the chances of maternal death. Researchers created an interview guide that directly assessed four issues regarding BKs left with village leaders in July 2005: BK distribution, explanation of BK item usage, BK item effectiveness, and birth outcomes during BK births. Only 2 of the 50 BKs were actually distributed in time for expecting mothers to use them during the birthing event.

Results:

Interviews with those women and several others who received and utilized BKs distributed in during this visit yielded data which led researchers to the following conclusions. 1) A more efficient and reliable BK dispersal system needs to be instituted in Rima Village; 2) BK distributors need to receive better and more expansive training in BK usage; 3) BKs, when used, were deemed helpful in providing hygienic and convenient births; 4) A baby's hat and blanket should be added to the BKs.

Medical Humanities

Mira L. Kistler, MS2

Preceptor:

Stephanie Brown Clark, M.D., Ph.D.

Assistant Professor of Medical Humanities

Department of Center for Ethics, Humanities and Palliative Care

University of Rochester Medical Center

Art and Alzheimer's: Pilot Project with Patients at the Memorial Art Gallery

Abstract:

Alzheimer's disease is characterized by a progressive deterioration of memory and cognitive function that results in neuropsychiatric symptoms and the inability to perform the daily tasks of living. Treatment for Alzheimer's involves both pharmacologic and non-pharmacologic therapies such as art and music therapy. We present here the results of a pilot program for Alzheimer's patients involving art observation at the Memorial Art Gallery (MAG) in Rochester, New York. This program is based on the Meet Me at MOMA program at the Museum of Modern Art in New York City. Using information from observations of the Meet Me at MOMA program, as well as interviews with its founders, we designed and implemented a pilot program using slides of paintings from the MAG collection for six Alzheimer's patients at their residence facility. Evaluation of the pilot involved observation of participants' reactions to the program and caretaker feedback. Results of the pilot show improvements in participants' moods and verbal expressions and indicate a therapeutic value for art observation in facilitating discussion about personal interests and life experiences.

Results:

Results of the pilot for this museum program show improvements in participants' moods and verbal expressions and indicate a therapeutic value for art observation in facilitating discussion about personal interests and life experiences.

Medical Humanities

Brooke Shuster, MS4

Preceptors:

Stephanie Brown Clark, M.D., Ph.D.

Assistant Professor of Medical Humanities

Department of Center for Ethics, Humanities and Palliative Care

University of Rochester Medical Center

Suzanne Crengle, M.D.

Maori Health Unit University of Auckland

Auckland, New Zealand

Secondary Prevention of Ischemic Heart Disease and Ischemic Stroke in Maori vs. non-Maori, Auckland, New Zealand

*"He aha te mea nui o te ao? Maku e kii atu he tangata, he tangata, he tangata."
What is the greatest treasure on earth? It is people, it is people, it is people.*

Cardiovascular disease is the leading cause of death in New Zealand, accounting for greater than four in every ten deaths across all ethnicities. According to Statistics New Zealand, on average, Maori life expectancy at birth is 8.5 years less than that of non-Maori. Maori have the highest rates of ischemic heart disease out of all ethnicities in New Zealand; additionally, they have the highest rate of hospital admissions for heart failure, representing nearly three times that of Europeans and other subgroups in the New Zealand population. Despite this inequity in the burden of disease, the rates of usage of medical treatments and interventions experienced by Maori do not match the elevated morbidity, leading to a significant disparity in life expectancy.

Hypothesis: The burden of ischemic heart disease is higher in the Maori population in New Zealand due to ineffective delivery of primary care services, including lack of or limited access of Maori individuals to the provided primary care services, lack of or decreased number of self-identified Maori primary care and hospital-based physicians, and decreased awareness of Maori cultural differences that affect care amongst non-Maori physicians. Institutional racism against Maori exists within New Zealand's medical system, which contributes to all three hypotheses listed above.

Methods: This was a randomized prospective cohort study. Patients at Middlemore Hospital in Auckland, New Zealand with acute admission for the following diagnoses were recruited: angina, myocardial infarction (MI), ischemic stroke (CVA), and transient ischemic attack (TIA). Upon recruitment, a survey was administered with each patient. This questionnaire focused on their view of their healthcare, as provided by their general practitioner (GP), including their usage of the primary health care system, limitations to access, their opinions of their GPs cultural competency skills, and ethnicity questions. At the same time, information was taken from the patients' hospital records, including age, height, weight, body mass index (BMI), smoking status, prescribed medications before and after discharge, surgical interventions completed during the admission, past medical history, and preventive services provided during the admission. Patients were again interviewed at twelve months after being discharged from their hospital stay for the above diagnoses; similar questions regarding their opinions of their primary health care and provider were asked at this time. Additionally, at twelve months post-discharge, the GP of each patient was also interviewed, which included questions on

where he or she received medical training, the office's system for following up on the above patients, and opinions on providing care for patients with ischemic heart disease and stroke. Data was also taken from the patient's records, regarding medications, interventions and preventive care that had been provided in the twelve month interim.

Results/Discussion: An initial analysis was completed using three groups of patients: Maori, Pakeha, and Other ("*Pakeha*" is a Maori term referring to individuals whose ethnicity is "New Zealand European"). In total, 540 patients will be interviewed by the end of the study. This analysis is a preliminary view of the first 200 patients recruited into the study. 98 Maori, 72 Pakeha and 30 "Other" patients were recruited. The average ages at the time of recruitment within the three groups were: 53.3 years for Maori, 65.7 years for Pakeha, and 58.2 years for Other. Many different factors were assessed during this study, with a resulting variety of outcomes. However, in terms of patient characteristics, the Maori patients in the study were younger at the time of their acute event, experienced higher rates of poverty, had lower levels of education, and had higher rates of diabetes. The analysis of the questionnaire results demonstrated that Maori were the most likely not to have a GP that they visit regularly for care, were more likely to not be able to afford primary care visits, were most likely to report that they "constantly" think about their own ethnicity, and were most likely to report that they had been treated unfairly by a health professional due to their ethnicity. On characteristics before admission, the Maori group had an average BMI that was significantly higher than the other two groups. During the hospital admissions, there were disparities in the quality of care provided to patients in each ethnic grouping, including differing rates of PCI, coronary artery bypass grafting (CABG), smoking cessation counseling, exercise advice, and medication prescription for the secondary prevention of further events.

Year-Out Research

Adeel A Abbasi, MS4

Preceptors:

Mehmet C. Oz, M.D.

Director of Cardiac Transplant Center

Columbia University College of Physicians & Surgeons/New York-Presbyterian Hospital

Dept. of Cardiovascular Surgery

Dr. Michael Argenziano

Director of Robotic Division, Cardiac Surgery,

Columbia University College of Physicians & Surgeons/New York-Presbyterian Hospital

Dept. of Cardiovascular Surgery

The Role of a Platelet Activating Factor Receptor Antagonist in Preventing the Development and Maintenance of Atrial Fibrillation via the Regulation of the TASK-1 Cell Membrane Channel, in an Animal Model of Post-Operative and Chronic Atrial Fibrillation.

Introduction:

Atrial fibrillation (AF) in the post-operative period has been reported to occur in 30-40% of patients following Coronary Artery Bypass Graft surgery, 37-50% after valve surgery, and in as many as 60% of patients undergoing combined surgeries. Although AF is usually self-limited, it may be associated with significant increases in post-operative morbidity, including embolic stroke, as well as increased in-hospital and long-term mortality.

Prophylactic therapy including beta blockers and amiodarone is effective in preventing AF in approximately one-half of these cases. However, a significant number of patients remain without adequate treatment. Therefore, development of a novel pharmacological therapy that could serve either as a primary treatment or as an adjunct to improve the success of current treatments would be a great advance. Moreover, a better understanding of the underlying biochemical and biophysical changes associated with AF might enable physicians to identify patients who are most likely to benefit from the available surgical or pharmacological interventions.

Aim:

In this study we will explore the underlying mechanisms of peri-operative AF, with the goal of developing novel therapeutic modalities useful in treating the disease. We propose to investigate the hypothesis that a molecule known as platelet-activating factor (PAF) contributes to the development and maintenance of AF via regulation of the TASK-1 cell membrane channel. Earlier studies in a canine model of chronic AF have found that there is a phosphorylation-dependent loss of function of the two-pore domain K⁺ channel named TASK-1, and that this is associated with arrhythmogenesis in the ventricle. We have recently extended these observations to a canine model of peri-operative AF. These results have suggested that dysfunction of the TASK-1 channel may also contribute to peri-operative AF. This study will make use of a well-established PAF receptor (PAFR) antagonist, CV6209. We have used this drug to block polymorphonuclear leukocyte-induced arrhythmias including AF in isolated canine ventricular myocytes.

Hypothesis:

Our hypothesis is that peri-operative AF is associated with phosphorylation and dysfunction of TASK-

1 channels which contributes to membrane instability and arrhythmogenesis. We have already shown that a signaling cascade initiated by platelet-activating factor (PAF) leads to the phosphorylation-dependent inactivation of the TASK-1 channel. The aim of this prospective randomized clinical trial is to determine if TASK-1 loss is reversible or preventable, and if pharmacological approaches to reversing or preventing the loss of TASK-1, such as the use of a PAF receptor antagonist, decreases the inducibility of peri-operative AF.

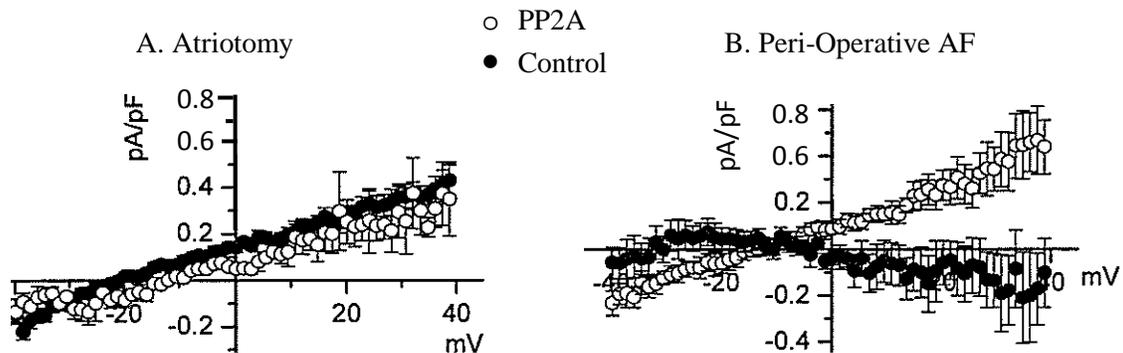
Method:

In this study, we will use an established model of post-operative atrial fibrillation to study the efficacy of the amiodarone patch. There will be three study groups, each of four dogs. The canine subjects will be randomized into three groups: (1) control in which no pharmacotherapy will be delivered, (2) PAFR antagonist-treated animals in which the animals will be pretreated with CV6209, and (3) PAFR antagonist-treated animals in which peri-operative AF will be stimulated and subsequently treated with a PAFR antagonist following induction of AF.

The study endpoints are (a) incidence of AF induction, (b) threshold of inducibility of AF, and (c) duration of induced AF. Compared with subjects receiving no prophylactic treatment, we predict that animals treated with PAFR antagonist will have lower incidence of peri-operative AF, higher threshold for induction, shorter duration of AF, and a lower percentage of phosphorylated TASK-1 channels.

The subjects will first undergo a right atriotomy, which will create an inflammatory cascade simulating open heart surgery. They will be survived for three days, and will then undergo pacing whereby AF will be induced using a programmable pulse generator. The parameters for AF induction will be recorded, and the subject euthanized. The right atrium will be excised to obtain cardiac myocytes for analysis of TASK-1 channel activity.

Results:



Discussion:

Analysis of data obtained from the first 3 subjects in the control arm have demonstrated that, like in the chronic model of AF, the TASK-1 channel is inactivated during peri-operative AF. The intracellular application of the serine-threonine phosphatase (PP2A) had no effect on TASK-1 current in the control myocytes (filled circles) but did rescue the current in cells derived from animals with peri-operative AF (empty circles). This supports our hypothesis that dysfunction of the TASK-1 channel is involved in peri-operative as well as chronic AF.

Year-Out Research

Frank Albino, MS2

Preceptor:

Michael Zuscik, Ph.D. Assistant Professor
Center for Musculoskeletal Research
University of Rochester Medical Center

BMP Signaling As a Potential Therapeutic Strategy for Reversing Cartilage Degeneration

Abstract

Mesenchymal stem cells are capable of differentiating into multiple cell types and thus may be used experimentally as precursors to chondrocytes. Previous experimentation indicates that articular chondrocytes participating in the process of osteoarthritis (OA) inappropriately express hypertrophic markers similar to chondrocytes undergoing endochondral ossification. Study of the factors/mechanisms that drive this maturation implicate a loss of transforming growth factor (TGF- β) signaling and enhanced BMP signaling as the central molecular mechanism that causes pathology. Interestingly, a blockade of enhanced BMP signaling reverses the expression of hypertrophy markers. Preliminary findings suggest that OA is caused by a shift in signaling dominance from the TGF- β pathway to the BMP pathway. Based on the importance of these signaling pathways in regulating chondrocyte phenotype in arthritis, we hypothesize that blockage of BMP signaling will inhibit the differentiation cascade in chondrocytic cells. To test this hypothesis we overexpressed the ubiquitin E3 ligase Smurf1, which inhibits BMP signaling via a degradation of BMP Smad signaling factors, and evaluated signaling activity using a 12XSBE Luciferase reporter in C3H10T1/2 chondrocytic cells. Confirming that Smurf1 can inhibit BMP signaling, Smurf1 transfected cells show a 50% decrease in signaling. The next step will be to evaluate the differentiation potential of cells with Smurf1 overexpression. Ultimately, Smurf1 may be the basis of a novel therapeutic paradigm leading to inhibition of chondrocyte maturation and decreased degeneration.

Year-Out Research

Vinit Amin, MS2
Samit Shah, MS2

Preceptor:
Arthur J. Moss, M.D.
Heart Research Follow-up Program
University of Rochester Medical Center

Genotype-Phenotype Aspects of Type-2 Long-QT Syndrome

John Castle; Han Goldenberg, MD; Wojciech Zareba, MD PhD; Coeli Lopes, PhD; Scott McNitt, MS;
Slava Polonsky, MS; Jennifer Robinson, MS

Background: Type-2 Long QT syndrome (LQT2) is caused by mutations involving the HERG-encoded cardiac potassium channel leading to arrhythmia-related events such as syncope and sudden death. In the present study we evaluated the risk associated with mutations located within prespecified domains of the HERG gene.

Methods: A multivariate Cox proportional hazards regression model was used to assess the independent contribution of mutation domains to the development of LQTS-related cardiac events (syncope, aborted cardiac arrest or LQTS-related death) in 440 LQT2 patients enrolled in the US portion of the International LQTS Registry.

Results: After adjustment for gender, QTc and β -blocker therapy, the risk of cardiac events was highest among patients with mutations in the transmembrane region (HR=2.45, $P<0.0001$) whereas no significant difference was shown between the N- and C-terminus ($p=0.17$). Further analysis of specific regions within the N- and C-terminus domains showed that the PAS (Per-Arnt-Ser) region of the N-terminus domain and the non-cNBD (cyclic nucleotide binding domain) region of the C-terminus domain were independently associated with a respective 74% ($p=0.041$) and 69% ($p=0.0039$) increase in the risk of LQTS related cardiac events during follow-up as compared with the cNBD region of the C-terminus domain.

Conclusions: This large genotype-phenotype study indicates that in LQT2, mutations located in distinct domains of the potassium channel confer a different risk of LQTS-related cardiac events during long-term follow-up.

Year-Out Research

Pam Choi, MS2

Preceptor:

Mary Katherine Santos, M.D.

Department of Pediatric Surgery

University of Rochester Medical Center

Retrospective Analysis of Open and Laparoscopic Appendectomies in the Pediatric Population

Abstract: Appendicitis is the most common cause of emergency surgery in children.

Surgical removal of the appendix via an open appendectomy has been considered the gold standard of treatment for almost a century. However, laparoscopic appendectomy has become more commonplace since its inception nearly two decades ago. Today, the advantages of either approach to appendectomy have been widely debated. Studies have reported a wide range of benefits for laparoscopic appendectomy, including faster healing and recovery and decreased postoperative pain. Other studies have found an increase in postoperative complications after performing a laparoscopic appendectomy on patients with complicated (i.e. perforated) appendicitis. We have conducted a retrospective analysis on all appendectomies performed on pediatric patients at Strong Memorial Hospital over the last four years in an effort to reveal any advantages of one procedure over the other in terms of length of stay, complication rate, and post-operative pain.

Results: There were a total of 606 appendectomies performed by the Pediatric Surgery Department from May 1, 2002 to April 30, 2006 at Strong Memorial Hospital. Of these, 162 cases were excluded as incidental appendectomies (i.e. appendicitis was not the primary reason for operation). Additionally, 6 patients were excluded due to age (cut off being 15 years old at the time of the operation). There were 438 appendectomies performed (265 open procedures and 173 laparoscopic procedures). There were no cases of mortality and 1 case of an accidental cut during an open appendectomy (serosal tear of the cecum). There was also 1 case of a conversion from laparoscopic to open procedure. Surprisingly, more complicated cases of appendicitis were treated laparoscopically.

Perforated/gangrenous appendicitis cases composed 17.3% of all laparoscopic procedures compared with 5.3% of all open cases. With the pathology of the appendix taken to account, univariate ANOVA revealed that there was no significant difference in length of stay, complication rate, or post-operative narcotic dosage between the laparoscopic and open groups.

Contrary to other studies, we have determined that laparoscopic appendectomies are equally efficacious to their open counterparts in cases of perforated or gangrenous appendicitis.

Year-Out Research

Matthew Daul, MS2

Preceptor:

Bradford C. Berk, M.D., Ph.D.

Senior Vice President Health Sciences Chief Executive Officer

University of Rochester Medical Center

Axl Contributes to Vascular Impairment in DOCA-Salt Induced Hypertension

Matthew Daul, Vyacheslav A. Korshunov, Michael P. Massett, and Bradford C. Berk
Cardiovascular Research Institute, and Department of Medicine, School of Medicine and Dentistry,
University of Rochester, Rochester, NY

Axl, a tyrosine kinase receptor, has recently been identified as a candidate gene in the development of salt induced hypertension via an integrated genomic-transcriptomic approach. Previously our group found that Axl is important in vascular remodeling. Here we investigate the role of Axl in the pathogenesis of hypertension in a deoxycorticosterone-acetate (DOCA) salt model. Hypertension was induced in Axl wild-type (Axl +/+) mice and Axl deficient (Axl -/-) mice employing uninephrectomy and subcutaneous implantation of a DOCA pellet. Mice were subsequently given 1% NaCl solution to drink in addition to normal chow for 6 weeks. Controls were uninephrectomized and received tap water and regular chow ad libitum. Systolic Blood Pressure (SBP) was measured using a non-invasive tail-cuff method and recorded 3 days before surgery and weekly thereafter. Axl +/+ DOCA mice developed and maintained SBP increases up to 30 mmHg compared to controls beginning at week 1. In comparison, Axl -/- DOCA mice SBP levels matched controls by 5 weeks time. Axl -/- mice gained weight faster following surgery compared to Axl +/+ counterparts. DOCA-salt increased relative kidney weight by 40% compared to controls similarly in both genotypes. Consistent with DOCA-salt induced hypertension Axl +/+ mice exhibited increased maximal responses to KCl and phenylephrine (2-3 fold) as well as increased sensitivity (ED50). In contrast, vasoconstriction in Axl -/- DOCA mice was attenuated compared to wild-types. Endothelium-dependent vasorelaxation (Acetylcholine) was impaired in Axl +/+ DOCA mice (-7.0 M) compared to Axl +/+ controls (-7.4 M) while in Axl -/- DOCA mice relaxation responses were augmented (-7.4 M) compared to Axl -/- controls (-7.1 M). Additionally, endothelium-independent vasorelaxation was improved in Axl -/-DOCA mice (-8.5 M) compared to Axl +/+ DOCA mice (-7.8 M). These data confirm the role for Axl as a key mediator of vascular impairment in salt-induced hypertension.

Year-Out Research

Stephanie A.M. Giannandrea, MS4

Preceptors:

Linda Chaudron, M.D., M.S.

Department of Psychiatry

University of Rochester Medical Center

Reproductive Losses and Perinatal Depression

Authors: Stephanie A.M. Giannandrea, BA; Linda H. Chaudron, MD, MS; Holly Wadkins, MA; Elizabeth Anson, BA; Kimberly Sidora-Arcoleo, MPH; Harriet J. Kitzman, RN, PhD

Introduction: Spontaneous and induced abortion, subsequent childbirth, and perinatal depression are common events in the lives of low-income, minority women, but there is virtually no literature on possible relationships between these factors.

Objectives: 1) To compare risk factors for perinatal depression in poor, predominantly minority women who have experienced pregnancy loss, defined as miscarriage, fetal death, stillbirth, and/or induced abortion, with women who have never experienced reproductive loss. 2) To compare risk factors for perinatal depression between women who have undergone induced abortion and involuntary pregnancy loss.

Methods: The original study was designed to validate screening tools for postpartum depression in low-income women across the first postpartum year. Women were recruited at pediatric well child-care visits from an urban pediatric clinic in an academic center. Cross-sectional data were collected from 194 women, including demographic information, questionnaires, depression screening tools, and the Structured Clinical Interview for the DSM IV (SCID). The current study is a preliminary secondary analysis using of original data from 153 women to explore the relationship between pregnancy loss and subsequent perinatal depression. Data were analyzed by chi square, t-test, and linear regression using SPSS 13 for Windows.

Results: Women who had experienced pregnancy loss did not differ significantly from women who had not in any demographic factors except older mean age. Women with a history of pregnancy loss were more like to be depressed during the first postpartum year after a subsequent live birth ($p=.019$). A history of prior spontaneous abortion did not significantly increase the risk of postpartum depression, anxiety, substance use, or PTSD in the year after delivery, although anxiety trended toward significance. History of induced abortion significantly increased anxiety and substance use in the first postpartum year, but did not increase the odds of depression or PTSD, although depression trended toward significance. A reproductive history of both spontaneous and induced abortion increased the odds of postpartum depression and anxiety, while PTSD and substance use trended toward significance.

Conclusions: Because women with a history of pregnancy loss are at increased risk for postpartum depression, they should be monitored closely for depression around the birth of a subsequent child. Follow-up visits could be scheduled during times of increased vulnerability to depression. In addition, earlier and more aggressive treatment should be considered in women with these risk factors.

Year-Out Research

Anthony L. Petraglia, MS4

Preceptors:

Berislav V. Zlokovic, M.D., Ph.D.

Zhenhua Wu

Zhihui Zhong

Meenakshisudaram Thiyagarajan

Tong Cheng

Department of Neurosurgery

University of Rochester Medical Center

Zhang Li

Michael Chopp

Department of Neurology

Henry Ford Health Sciences Center

Jose Fernandez

John Griffin

Department of Molecular and Experimental Medicine

Scripps Research Institute

Activated Protein C Inhibits tPA-Mediated Hemorrhage after Stroke in Rodents

Brain hemorrhage is a serious complication of tissue plasminogen activator (tPA) therapy for stroke. Here, we report that activated protein C (APC), a serine protease with direct neuroprotective activity, blocks tPA-induced brain hemorrhage after transient ischemia and embolic stroke in rodents. We used a mechanical stroke model with 45 min. middle cerebral artery occlusion (MCAO) followed by 24 hr reperfusion in 28-30g C57Bl6 mice. Vehicle, tPA, or tPA and mouse recombinant APC were administered via the femoral vein either during or after MCAO. Hemoglobin levels in the brain and volume of injury were then determined. Embolic stroke was induced by placing a single intact homologous clot at the origin of the MCA in 350-450g male Wistar rats. tPA was infused intravenously 4 hr after stroke in combination with APC or vehicle. We then performed behavioral measurements at 2 hr, 1 day and 7 days. We found that tPA infusion in mice subjected to focal transient ischemia resulted in brain hemorrhage in all studied animals and increased hemoglobin levels by 3.6-fold in the ischemic hemisphere. APC infused simultaneously with tPA or 3 hr post-tPA infusion blocked post-ischemic tPA-mediated bleeding and brain hemoglobin influx in a dose-dependent fashion. In addition, tPA significantly increased brain infarction in mice subjected to transient ischemia, whereas APC dose dependently reduced brain infarction in tPA-treated animals. In the rat embolic model, we found that tPA induced significant microscopic hemorrhage after 1 and 7 days, whereas APC in combination with tPA reduced hemorrhage by > 90% and 80%, at 1 and 7 days respectively. Also, APC alone or in combination with tPA significantly reduced brain injury at 1 and 7 days and improved functional recovery compared to vehicle-treated or tPA-treated animals. Although tPA thrombolysis is beneficial for stroke, its neurotoxicity and hemorrhage need to be controlled. The present study demonstrates that APC controls tPA-mediated hemorrhage and thus could be an ideal candidate for tPA adjunctive therapy in stroke

Year-Out Research

Clinton Protack, MS3

Preceptor:

Mark G. Davies, M.D., Ph.D.

Department of Vascular Surgery

University of Rochester Medical Center

Urokinase-Induced Smooth Muscle Cell Migration Involves the Mammalian Target of Rapamycin

Purpose: To determine a role for the mammalian target of rapamycin (mTOR) in urokinase (uPA)-induced smooth muscle cell (SMC) migration, and to examine specific kinase pathways that may act downstream of mTOR to influence the response of SMCs to uPA.

Background: Vascular SMC migration is an important component of the development of intimal hyperplasia. During tissue remodeling, uPA is one of the key serine proteases involved and stimulates SMC migration in vitro. Rapamycin is an antifungal and immunosuppressant that inhibits mTOR, which regulates p70S6 kinase (p70S6K) activity. We examined the effect of rapamycin on uPA induced SMC migration, the activation of mTOR and p70S6K and its effects on MMP-2 expression.

Methods: Rat arterial SMCs were cultured in vitro. Linear wound and Boyden microchemotaxis assays of migration were performed in the presence of uPA (1-100 nM) with and without rapamycin (1-10 nM). Additional studies were performed in the presence of the PI3-Kinase inhibitor LY294002 (10 nM). Western blotting was performed for phosphorylated and total mTOR and p70S6K after stimulation with uPA (10 nM) with and without rapamycin. MMP-2 activity determined by zymography.

Results: uPA stimulated migration of SMCs in both the linear wound assay ($p < 0.01$) and in the Boyden chamber ($p < 0.01$); these responses were inhibited completely by rapamycin in a concentration dependent manner. uPA stimulated phosphorylation of mTOR and p70S6K (2-fold increase over control for both, $p < 0.05$). These responses were inhibited by the presence of the PI3-K inhibitor ($p < 0.01$). Rapamycin completely inhibited both mTOR and p70S6K phosphorylation. uPA induced expression and activity of MMP-2 was markedly inhibited by the presence of rapamycin.

Conclusions: uPA-induced SMC migration is mTOR dependent. Activation of mTOR and p70S6K is PI3-K dependent. Inhibition of mTOR and p70S6K resulted in a decrease in MMP-2 expression and activity. Understanding the basic mechanisms of cell migration will allow therapeutic intervention for restenosis.

Year-Out Research

Deanne Mraz Robinson, MS3

Preceptor:

Chin-To Fong, M.D.

Department of Pediatrics and Genetics

University of Rochester Medical Center

The Genetic Epidemiology of Prematurity

Deanne Mraz Robinson, CC3, Guillet R, M.D PhD., Fong CT, M.D.

Background: Preterm delivery prior to 37 weeks occurs in approximately 10% of live births and is a significant health care issue as it is the leading cause of newborn death; survivors can face lifelong health and/or developmental problems. Risk factors for prematurity include: previous preterm birth, smoking in pregnancy, multiple gestations, and certain maternal infections. Little is known about the genetic factors that may contribute to prematurity.

Objective: To better understand the epidemiology of prematurity in families through examining the familial nature of its occurrence.

Design/Methods: Study subjects were all mothers (≥ 18 yrs of age) who delivered preterm infants cared for in the NICU at Golisano Children's Hospital at Strong. Mothers were interviewed using a standardized questionnaire to collect demographic data on mother and infant, including gestational and maternal age at birth of the baby, race, parity, pregnancy history, prenatal care, and socioeconomic status. A detailed family history spanning three generations was obtained to ascertain the gestational ages of the index infant's relatives.

Results: Eighty-five mothers were approached for the study, seventy-two of which consented to the interview. Taking the regional rate of preterm delivery to be 10 %, we calculated the relative risk ratio for premature birth among siblings (λ_s) and parents (λ_p) of the preterm infants. Among the 35 siblings of these preterm infants, 16 were premature, yielding a λ_s of 4.57. Among the 116 parents of the preterm infants, 10 were premature, yielding a λ_p of 0.86. For the siblings, the attributable risk (AR) can be calculated to be 78.1 %, whereas that for the parents is -16.3%. Of the 10 preterm parents, 8 were mothers and 2 were fathers. This allowed us to determine that the relative risk ratio for mothers (λ_m) and fathers (λ_f) are 1.38 and 0.34, respectively. The AR for mothers is 27.5%.

Conclusions: In this small pilot study, we demonstrated a trend towards an increase in the incidence of premature birth among the siblings and mothers of preterm infants, with the relative risk for the siblings being higher than that of the mothers. Since there is 50% sharing of alleles between both sibling/sibling and mother/child pairs, our results strongly suggest that maternal factors other than shared-alleles also contribute to preterm delivery. While the sample size is still small, these observations nevertheless raise interesting questions about the familial nature of preterm delivery, and may inform studies of the genetic contribution to prematurity.

Year-Out Research

Rachel Rubin, MS4

Preceptor:

Arnold Matlin, M.D., FAAP

Clinical Assistant Professor of Pediatrics

University of Rochester School of Medicine and Dentistry Department of Pediatrics

Diabetes Education and Public Health in El Sauce, Nicaragua

Abstract: The prevalence of type II diabetes is increasing in developing countries in Latin American countries as rural populations migrate to urban areas in search of work, a decreasing proportion of the population participates in manual labor, and the average diet become more heavily processed. Although statistics are not available for the prevalence of type II diabetes in Nicaragua, WHO statistics from other developing nations in Latin America, specifically Cuba and Bolivia, indicate increases in prevalence in both rural and urban populations since the 1980s. I participated in a six-month student fellowship at the Centro de Salud in El Sauce, Nicaragua, a Nicaraguan government-run primary health care center serving a population of 35,000. During the time period from February through June, 2006, I developed and implemented an education program for patients with type II diabetes, the Club for Diabetics, in which participants met to discuss a weekly theme and share experiences. The Club for Diabetics emphasized self-care and adapting the principles of nutrition for diabetics to a population with severely limited economic resources, food insecurity, and minimal literacy skills. Weekly themes included basic pathology of diabetes, prevention and management of complications, nutrition for diabetics, heart health, exercise in diabetes, hypertension, and skin care. Other fellowship activities included participating in clinics for patients with chronic diseases, participating in clinics for women and children at rural health outposts, and assisting with public health and sanitation activities, including: census taking, vaccination campaigns, and nutrition assessment in children.

Results: Although limited in number (six), participants reported a high degree of satisfaction with the Club for Diabetics, increased knowledge of basic disease mechanisms, improved understanding of the effects of carbohydrates on glycemia, and improved ability to follow a lower-carbohydrate diet.

Acknowledgements

Thank you to all the mentors and preceptors who gave their time and support to work with University of Rochester Medical Students.

A Special thank you to Dr. Nancy Chin for her expertise in preparing International Medicine students for their field experiences.

Thank you to the Dean's Office for their support and funding of student research.

Thank you to Nancy Janson (Director), Margaret Christian, and Ellen Poole in the Offices for Medical Education's Financial Aid Office for their support

Special acknowledgement and thank you to Mary Christian for putting this journal together.

Basic Science and Clinical Research Faculty Advisory Committee Members

Richard Reichman, M.D. (Chair)	Denham Ward, M.D.
Tom Pearson, M.D., Ph.D	Steve Lurie, M.D., Ph.D.
Manish Shah, M.D.	Linda Chaudron, MD
Robert Holloway, M.D.	Jane Greenlaw, JD George Schwartz, M.D.

The Community Outreach Faculty Advisory Committee Members

Nancy Chin, Ph.D., MPH (Chair)	Jonathan Klein, M.D.
Noelle Andrus, Ph.D.	Brenda Lee, M.Ed.
Theodore Brown, Ph.D.	Scott Mcintosh, Ph.D.
Laurie Donahue, M.D.	Jenny Speice, Ph.D.
Kevin Fiscella, M.D.	Sally Trafton, J.D.
Laurence Guttmacher, M.D.	Richard Kennedy, M.D.

The International Faculty Advisory Committee Members

Ralph Jozefowicz, MD. (Chair)	Brooke Lerner, Ph.D.
Nancy Chin, Ph.D., MPH	Katherine O'Hanlon, M.D.
Glenn Currier, M.D.	Mark Shelly, M.D.
John Hansen, Ph.D.	Giovanni Schifitto, M.D.
Michael Keefer, M.D.	Steve Schultz, M.D. David Korones, M.D.

The Medical Humanities Faculty Advisory Committee Members

Stephanie Brown-Clark, M.D., Ph.D. (Chair)	Brenda Lee, M.Ed. Theodore Brown, Ph.
Timothy Quill, M.D.	Jules Cohen, MD.
Jane Greenlaw, JD	

The Center for Advocacy, Community Health, Education and Diversity
Adrienne Morgan, MS (Co-Director)
Gladys Pedraza-Burgos, MS (Co-Director)
Mary Christian
Janet Koslow