

Karyn Winkler

Advisor(s): Jack Moallem
Rauno Joks

Severe Thrombocytopenia with Upper GI Bleed after MMR Vaccination

Adverse effects of MMR vaccination, mostly self-limited and benign, are reported. Fever in up to 15% of vaccinees, transient rash in up to 5%, febrile seizures, as well as mild lymphadenopathy are reported. Thrombocytopenia after MMR vaccination is reported in 1:25,000 to 1:2,000,000. There is no report of thrombocytopenia resulting in severe hemorrhagic complications or death in immunocompetent recipients. Infrequency with which it occurs makes it a challenging diagnostic task for practitioners. A 13 month old male presented to the emergency department due to 2 episodes of bloody vomitus. 2 days prior he had fallen and sustained a rapidly enlarging hematoma on his forehead. 10 days prior he was vaccinated with the MMR vaccine. There was no reported history of fever or recent upper respiratory illness. Examination in the ED demonstrated a fussy child, HR 145, RR 36, T 100.2F, with a 5 cm hematoma on the forehead, a hemorrhagic lesion on the upper lip, gingival bleeding and multiple petechiae on the upper/lower extremities. Laboratory investigation was significant for platelet count of 5K/uL, Hgb 8.4 g/dL and Hct of 24.7% on CBC. Indirect Coombs test and Stool Guaiac were positive. In PICU his hemoglobin further dropped to 4.0 g/dL, requiring transfusion. Bone marrow aspiration revealed absence of lymphoblasts with increased megakaryocytes and red blood cell precursors. He was treated with IVIG 1g/kg/day for 2 days and Methylprednisolone 4mg/kg/day for 4 days then continued on PO prednisone 2mg/kg/day. CBC on the 7th day of admission showed platelets of 311 K/uL, and increase of hemoglobin hematocrit to 9.4 g/dL and 28%. ITP after MMR vaccination typically occurs within 6 weeks of vaccination. Mild bruising and petechiae are common. Hospitalization is rarely required. Transfusion is required in 1 of 1.8 million vaccinees. This is the first report of thrombocytopenia resulting in severe hemorrhagic complications in an immunocompetent recipient of the MMR vaccine.

Jonathan Mazer

Advisor(s): Dennis Dimaculangan

Sonographic evaluation of lumbar interlaminar space opening in a variety of patient body positions for optimal neuraxial anesthesia delivery.

Study Objective: To find the position that provided the widest L3-L4 interlaminar space opening and the most comfort when assumed by a subject. Design: Pilot Study. Setting: Operating room. Patients: 32 healthy volunteers. Interventions: The L3-L4 interlaminar space was measured on volunteers as each assumed a baseline position (sitting upright) and five study positions: 1) sitting in fetal position ; 2) sitting on a table tilted at 30 degrees; 3) sitting while hugging an exercise ball; 4) sitting with mid-calves on the table's edge; 5) lying on one side in fetal position. Interlaminar space measurements were analyzed to determine which position resulted in the largest interlaminar space compared with baseline. The comfort level while assuming each position was rated by subjects using a visual analog scale from 1-10. Main Results: The means of the interlaminar openings in all study positions were significantly different from baseline, with the "sitting fetal" having the greatest difference, (1.32mm, $p < 0.001$), followed by "hugging a ball", (0.94mm, $p < 0.001$) and "lying fetal", (0.92mm, $p < 0.001$). Mean visual analog scale scores for comfort showed that "hugging a ball" (7.8/10), "lying fetal" (7.5/10) and "sitting fetal" (7.2/10) positions had the highest ratings. Conclusions: Ultrasound measurements carried out on 32 subjects showed that the "sitting fetal", "lying fetal" and "hugging a ball" body positions provided the widest L3-L4 interlaminar space openings. These three positions were also found to be the most comfortable.

Diana Klopsis

Advisor(s): Rebecca Twersky
Stephan Kohlhoff

Quality Control Review of the ASA Physical Status (ASA-PS) Classification of Patients Undergoing Moderate Sedation by Non-Anesthesiologists

Rationale: ASA physical status (ASA-PS) is a standard scale widely used by anesthesiologists to communicate preoperative health status and risk. Reliability of the ASA-PS has been studied and criticized. Non-anesthesiologist physicians/nurses also commonly use ASA-PS in their assessment prior to moderate/deep sedation outside the OR. Since higher ASA-PS means greater risk, some facilities limit non-anesthesiologist-directed sedation to those with low ASA-PS. SEDASYS®, a recently FDA-approved computer-assisted sedation device for use by non-anesthesiologists, is limited to ASA-PS 1 and 2 patients. Assignment of high ASA-PS may require case cancellation or anesthesiologist consultation, but underscoring may lead to consequences if sedation isn't tolerated. This study aims to assess agreement in ASA-PS assigned by non-anesthesiologists compared with two anesthesiologists blinded to non-anesthesiologists' assignments.

Methods: A retrospective chart review of adult patients undergoing procedural sedation at SUNY DMC 2007-2012 was performed. Diagnosis, procedure, age, comorbidities, and ASA-PS assigned by non-anesthesiologists were tabulated for 764 observations. Using this data, two anesthesiologists blinded to ASA-PS assigned their own ASA-PS.

Results: ASA-PS scoring by non-anesthesiologists was substantially lower than scoring by anesthesiologists. Inter-rater reliability of ASA-PS by non-anesthesiologists vs. each anesthesiologist using weighted Kappa statistic revealed no agreement (weighted Kappa +0.02, +0.04 respectively). Inter-rater reliability between the two anesthesiologists was low to moderate (+0.32) with most discrepancies observed between scores 3-4 (if 3-4 pooled, +0.50).

Discussion: Agreement in ASA-PS scores between non-anesthesiologists and anesthesiologists is very weak, with non-anesthesiologists scoring substantially lower. This may suggest a need for focused education, especially with emergence of new systems like SEDASYS® requiring lower ASA-PS.

Iris Mizrahi

Advisor(s): Jennifer Baxter

Abstract: Timing of Prophylactic Antibiotics for Caesarean Deliveries

Rationale: Almost 33% of women in the United States undergo caesarean delivery (CD). CD is often associated with an increased risk for postpartum infection compared to vaginal delivery. Post-postpartum infections contribute to prolonged hospital stays, increased maternal morbidity, scarring, disturbed body image, interrupted family processes and early discontinuation of breastfeeding. To prevent complications to both mother and baby during CD, the use of prophylactic antibiotics (PAB) is widely endorsed. However, variations exist in the timing of PAB administration: before the incision or right after umbilical cord clamping.

Methods: Current evidence was compared to a policy of a local hospital. A literature review was conducted using multiple databases looking at primary research and systematic reviews and using the following keywords: “antibiotics”, “prophylaxis”, “caesarean delivery”, “c-section”, “infection”, “pre-incision” and “cord-clamping”. 11 primary sources and 6 systematic reviews dating from 2007-2015 were used, excluding multiple dose or long term AB use trials.

Results: There was no definitive evidence about the best timing, that is, prior to surgery or right after umbilical cord clamping. There are no significant differences in maternal morbidity and mortality when comparing the timing and timing has no negative effect on neonates.

Discussion/Significance: A local hospital policy does not reflect the lack of consensus in the literature as it guides practitioners to use pre-incision PAB only. Thus additional research is needed to ensure a pre-incision PAB only policy is best for patients and patient outcomes.

Marina Moiseyeva


Advisor(s): Jennifer Baxter

Assessment of Female Sexual Health by Advanced Practice Nurses in Primary Care Setting

Rationale: Female Sexual Dysfunction (persistent, recurrent problems with sexual response or desire) affects an estimated 43% of women in the United States. However, evidence suggests Advance Practice Nurses (APNs) may not be adequately assessing FSH. Barriers and facilitators to FSH assessments have not been studied thoroughly, and only one research study could be found examining the FSH assessment practices of APNs.

Methods: The proposed study will use grounded theory to explore and describe the process of the FSH assessment from the perspective of APNs to develop a substantive theory that explains the process of APN FSH assessment. In particular, the study will explore (a) barriers preventing APNs from initiating and completing sexual health assessments, (b) facilitators to successful completion of assessments, (c) frequency of female sexual health history assessments by APNs in the primary care setting, and (d) perceptions of the assessment from the providers' perspective. This study will be conducted in 3 community-based health clinics in New York City. Theoretical sampling will be used to ensure data saturation. Inclusion criteria are: (1) New York State certified APN; (2) current practice at community-based health clinics in Brooklyn, NY; (3) Care for cis-gendered female patients ages 18 and older receiving their primary care from the APN. Demographic characteristics will be collected including clinical background, working conditions, and sexual health assessment experience. Semi-structured interviews will be digitally recorded and transcribed verbatim. Data will be analyzed until themes emerge.

Results: This study is in the proposal stage and thus findings are not yet available.

Discussion/Significance: The results will provide a description of the current FSH assessment process among APNs, which may provide valuable groundwork to improve clinical practice and contribute to better health outcomes for female patients in the primary care setting. 

Dominique Juste

Advisor(s): Meriam Caboral

Role of Mental Practice on Motor Recovery among Stoke Patients: A Proposed Study

Rationale: Brain capacity and capability are recognized as the most important aspect of post-stroke recovery. Neural plasticity can change central nervous system structure and function. Mental practice (MP), a technique in which physical skills can be cognitively rehearsed in a repetitive manner, is effective for learning motor skills. MP is suggested to induce neural plasticity. Neuroimaging studies have shown that MP involves changes in neural functions and structures resulting in improved motor performance. International studies suggest that MP with conventional stroke rehabilitation (CR) enhances further motor recovery however they were limited by small sample size. Few studies were conducted on the use of MP on post-stroke recovery in the US where socio-cultural factors might differently affect MP's effectiveness.

Methods: An experimental study design will be used. 90 participants ages 40-60 years who experienced ischemic stroke with both upper and lower motor function deficits, no significant comorbidities and a Mini-Mental State Exam score of >18 will be recruited from a rehabilitation center in an urban city. Participants will be randomly assigned to either the MP group or the CR group. In addition to the usual rehabilitation protocol, the MP group will receive repeated training sessions on how to perform MP from a physical therapist. The Action Research Arm and the Fugl-Meyer Assessment will be used to assess motor recovery of upper and lower extremities at 1, 3 and 6 months. Repeated measures of ANOVA will be used to analyze the data.

Results/Significance: Results from this study may provide more definitive evidence on the applicability and effectiveness of MP for post-stroke patients. Advanced practice nurses working in rehabilitation would utilize MP in their practice to improve patient outcomes.

Jackie Ehrlich

Advisor(s): Meriam Caboral-Stevens

Centering Pregnancy and Prenatal Health Behaviors: A Proposed Study

Rationale: The US ranks low on worldwide indices of maternal child health. Prenatal behaviors are practices such as nutritional intake, exercise, weight gain, use of alcohol and tobacco, childbirth education, and prenatal care, that impact perinatal outcomes. Centering Pregnancy is a model of group prenatal care designed in large part to support healthy prenatal behavior, with emphasis on increased knowledge and participation in self-care. However, to date, studies are limited and results are conflicting as to the impact of CP on health behaviors.

Purpose: Using Pender's Health Promotion Model, the purpose of this study is to determine if CP is linked with improved prenatal behaviors, an intermediary factor in perinatal outcomes.

Method: A randomized controlled trial will be used. Two hundred forty eight English-speaking primigravid women at maximum of 12 weeks gestation, ages 18-40, and with no high-risk medical and obstetrical conditions will be randomly assigned to either the CP or traditional prenatal care group. Study participants will be recruited from two clinics that are approved CP sites. Lindgren's Health Practices in Pregnancy Questionnaire II will be administered at first and last prenatal visits to assess the degree to which pregnant women exhibit behaviors in line with the six healthy goals. Scores will serve as a measure of overall prenatal health practices. Group means will be compared. Data will be analyzed using t-tests and chi-square.

Results/Significance: Findings from this study may provide more robust evidence for the use of CP to improve prenatal behaviors.

Ermias Ghebreyesus

Advisor(s): Meriam Caboral-Stevens
Joseph Jennas

Comparison between 1 MAC of Sevoflurane versus 1/2MAC of Nitrous Oxide added to 1/2 MAC of Sevoflurane effect on Mean Arterial Pressure.

Rationale: One of the challenges in anesthesia is finding the right balance of medications to reduce adverse effects. While under anesthesia, maintaining a mean arterial pressure (MAP) of ≥ 60 mmHg is necessary in perfusion of vital organs. For over 100 years, the use of inhaled volatile anesthetics, such as Nitrous oxide (NO) and Sevoflurane, is central to anesthesia practice. Minimum alveolar concentration (MAC) is the standard measures of potency for all volatile anesthetics - the lower the MAC value, the more potent the anesthetic.

Research question: "Does one minimum alveolar concentration (MAC) of Sevoflurane causes a greater decrease in mean arterial pressure (MAP) compared to the use of one-half MAC of nitrous oxide added to one-half MAC of Sevoflurane in patients undergoing laparoscopic cholecystectomy?"

Method: Guided by Betty Neumanns' Open Systems Theory, a prospective RCT study will be conducted. Forty participants ages 20-40 years old, American Society of Anesthesiologist Class I and II, no contraindications to both NO and Sevoflurane will be evenly randomized into 2 groups. Both groups will be induced and intubated using similar anesthesia drugs but will be maintained with either with one MAC (2% concentration) of Sevoflurane (Group A) or one-half MAC (1% concentration) of Sevoflurane and one-half MAC (50% concentration of NO (Group B). During the maintenance phase, the MAP will be measured every 5 minutes, averaged and compared from the baseline for both groups. Descriptive statistics and T-test will be used to analyze these data.

Results and Significance: What we might find in this study is that the addition of NO to Sevoflurane will minimize the decrease in MAP compared to using Sevoflurane only. The hemodynamic effect on MAP along with the beneficial effects on pain management, and lower cost will encourage nurse anesthetist to incorporate NO more frequently in their management.

Chao Jin Jin

Advisor(s): Meriam Caboral-Stevens

Postpartum Depression and Primiparous Women of Advanced Age.

Background/Rationale: About 13% of new mothers experience postpartum depression (PPD) within the first 12 weeks after giving birth. In recent years, women have delayed childbirth into much later years. Statistics have shown a steady increase in childbirth for women over 40 years of age. Women of advanced age have slightly higher scores of psychological distress. Healthcare professionals perceive older mother to have more problematic adjustments, which puts them at higher risk for PPD.

Purpose: To explore the incidence of PPD in primiparous women over 40 years old.

Conceptual framework: Meleis' Transition Theory will be used to guide the study. The theory deals with people going through transition process from instability to stability, that last a lifespan, by utilizing their personal experience, environment, community and society, Pregnancy is an event that could pose instability in a woman's life and there are mediating factors that influence their transition process including PPD, which could impact their adjustment after pregnancy.

Method: A comparative study design will be used. One thousand two hundred and fifty women who gave birth to healthy singleton babies will be recruited at 6-weeks postpartum from the pediatric and obstetric units of a large urban hospital. Study participants will be divided into 2 groups: > 40 years of age and ≤ 40 years of age. Postpartum depression will be measured using the 10-item Edinburgh Postnatal Depression Scale, a valid and reliable tool. Baseline data will be collected at enrollment (6 weeks postpartum) and will be followed up every 3 months for nine months. Data will be analyzed using Pearson Chi square test.

Results and Significance: Findings from this study may provide information on the incidence of PPD in primiparous women over 40 years of age. If the incidence of PPD in primiparous women over 40 is established, advanced practice nurses could be advised to increase screening older postpartum women for PPD.

Javier Martinez

Advisor(s): Meriam Caboral-Stevens
Joseph Jennas

A Proposed Study to Examine the Use of Nicotine Patch for Post-operative Pain Relief in Healthy Individuals

Rationale: An important part to post-operative pain management is to provide maximum pain relief while minimizing adverse effects of a single agent. Opioids are the most common drugs used for post-op pain relief. The use of nicotine patches in conjunction with opioids is an unconventional measure for post-operative pain relief. Applying nicotine patches prior to surgery has been shown to decrease the amount of opioids use post-operatively. Although nicotine is a known potent vasoconstrictor, it also has anti-inflammatory properties that could reduce pain.

Purpose: In healthy patients undergoing laparoscopic cholecystectomy, the use of transdermal nicotine patches will decrease the amount of opioids use to achieve adequate post-op pain control compared to those who did not receive a nicotine patches.

Method: A randomized, double-blind study will be conducted. 270 healthy, males and females, ages 20-40 years old, non-smokers, and with American Society of Anesthesiology Classifications I-II will be recruited from an urban hospital in Brooklyn. Study participants will be randomly assigned into Group AF (experimental) – who will receive a 21mg nicotine patch prior to start of procedure, and Group JM (control) will receive placebo patch; the patches will stay for 24 hours. A numeric pain scale will be used to assess to the severity of post-operative pain and post-anesthesia care nurses will monitor pain at 1 hour post-op and every 4 hours for 24 hours. The amount of opioids used will be taken from medication administration flow sheet. Data will be analyzed using Mann Whitney test.

Results and Significance: One of the roles of nurse anesthetists is to provide pain relief. Results from this study will provide additional information on the use of nicotine patch for pain relief in healthy patients.

Atinuke Olusanya

Advisor(s): Meriam Caboral-Stevens

A Proposed Study to Examine the Effect of TENS on Postoperative Nausea & Vomiting after Elective Gynecological Surgeries under General Anesthesia.

Rationale: Postoperative nausea and vomiting (PONV) remains one of the major anesthetic problems following general anesthesia (GA). The incidence of PONV is 3x higher in women than men. Drugs such as Ondansetron, an antiemetic, have not been entirely effective in preventing or treating PONV and have significant side effects. Transcutaneous electrical nerve stimulation (TENS), a non-pharmacologic technique closely related to acupuncture or acupressure, is a device with an electronic stimulus generator that transmits electricity to stimulate the area of the wrist (P6), which corresponds to the emetic center of the brain. TENS have been used to control PONV however studies have not been definitive.

Purpose: To examine the effect of using TENS at the P6 acupoint as adjunct to Ondansetron in reducing PONV in women undergoing elective GYN surgeries under GA.

Method: An RCT study will be conducted. Seventy women ages 18-50, ASA Class I or II, non-smoker, with no history of motion sickness and undergoing elective GYN surgery under GA at a large urban hospital will be recruited and divided into two groups: the Ondansetron with TENS (Group T) and Ondansetron without TENS (Group O). Both groups will receive Ondansetron 8mg intravenously before skin closure. TENS will be started after women recovers from anesthesia. Group T will receive one 30-minute treatment of TENS via active self-adhesive electrodes delivered by the researcher until the patient feels numbness, tingling or fullness sensation. Group O will have self-adhesive electrodes applied but no TENS stimulation. The Rhodes Index of Nausea, Vomiting and Retching (RINVR) will be used administered by recovery room nurses to measure PONV at 30 min. at 2, 4, 6, 10, 12, 18 and 24 hours post-op.

Results and Significance: The results may identify whether the use of TENS is an effective adjunct to drug therapy in this target population. It also provides nurse anesthetists treatment options for women experiencing PONV.

Meriam Caboral-Stevens

Advisor(s):

A Pilot Study on the Usability of a Health Web Site by Older Adults

Background: Older adults are the fastest growing internet users. The confluence between age and technology could present challenges in interface. Barriers include cognitive and functional limitations related to aging, literacy and access. Issues related to interface could be addressed through usability evaluation/testing. Usability refers to the fit between technology and user..

Purpose: To test the usability of a health web site in older adults.

Conceptual framework: A U.S.A.B.I.L.I.T.Y. Model© was developed from integration of diverse theories and concepts. The basic tenet of the conceptual model was that older adults and/or those with low or limited literacy will utilize a usable website for their own health information. Four determinants of usability were: efficiency, learnability, perceived user experience and perceived control.

Method: A nonrandomized, pilot study of 30 African-Americans, ≥55 years with diagnosis of HF were enrolled to watch a 30-minute interactive educational website on “Congestive heart failure.” A 25-item U.S.A.B.I.L.I.T.Y. Survey© was constructed to measure usability. The newly developed instrument has acceptable face and content validity and reliability.

Results: The study cohort consisted of 60% males, mean age of 67 ±9 years, average year of HF diagnosis- 6 years, mean EF 32.9%, and 43% had NYHA-FC I. Mean literacy score was 6.3 ± 2.4, and about half attended high school or less. Seventy-three percent were novice computer users and only 30% have computers at home. Average time in completing the task was 37.62 min ±14.3; shortest time - 22 min. and the longest was 88 min. The usability score was 106 ± 17. **Conclusion:** The study showed that regardless of literacy, education and computer expertise, older African-Americans with HF found a health web site usable. Technology can be an invaluable resource for older adults to use and learn which can increase patient knowledge thus facilitating patient engagement.

Hanna King

Advisor(s): Steven Levine
Coltilde Balucani

Women perceive differences in stroke prevention care based on their primary care physician's specialty

Background: Women have higher lifetime risk of stroke than men. Many women rely solely on their Ob/Gyn as their PCP; however, there are no data on women's perceptions of stroke prevention (SP) care by their Ob/Gyn.

Objectives: To explore (1) women's perceptions of SP based on their PCP's specialty; (2) if age influenced women's selection of PCP specialty; and (3) women's awareness of stroke prevalence and preferences for SP care.

Methods: We surveyed 245 women at Ob/Gyn (n=143) and PCP (n=102) clinics. Surveys consisted of 16 questions on demographics, awareness of stroke prevalence, stroke risk factors, physicians regularly visited, preferences for SP and SP care received. Kruskal-Wallis & Mann-Whitney tests were used to compare the distribution of ordinal variables and age. Fisher's exact test was used to test for an association between categorical variables. Cochran-Mantel-Haenszel test was used to determine associations, adjusting for age groups.

Results: We found a difference ($p < 0.0001$) in the mean age of women who only visited an Ob/Gyn ($31.2 \text{ yrs} \pm 7.3$) vs. Ob/Gyn+PCP (44.0 ± 16.3) vs. PCP only (55.7 ± 17.7). Women visiting only Ob/Gyns were less aware of stroke prevalence than those in other groups ($p = 0.01$). Fewer stroke risk factors were reportedly discussed by Ob/Gyns compared to PCPs ($p = 0.02$). Women reported receiving fewer tests for BP (RR 0.75, 95%CI 0.63-0.89, $p < 0.001$), cholesterol (RR 0.54, 95%CI 0.36-0.81, $p = 0.003$) and diabetes (RR 0.69, 95%CI 0.48-0.98, $p = 0.04$) from Ob/Gyns vs. PCPs. Women preferred addressing SP with their non-Ob/Gyn PCP (69.1%) vs. their Ob/Gyn (1.8%) vs. no preference (29.0%).

Conclusions: Ob/Gyns are perceived to provide less SP care than PCPs. However, most women would prefer to address SP with their non-Ob/Gyn PCP. Women who visit only an Ob/Gyn were younger and less aware of stroke prevalence than women who visited other PCPs. This surrogate approach to actual SP care evaluation suggests a need for assessing Ob/Gyn practices in SP.

Racquel Brereton

Advisor(s): Janet Rosenbaum

Assessing the association of frequent marijuana use and depression

Introduction: Data on the adverse health effects of marijuana use are still evolving. Previous research suggests a significant association between frequent marijuana use and depression. Understanding this association is increasingly becoming relevant, considering the wide use of marijuana and its projected legalization in New York City. The aim of this study is to assess the association of frequent marijuana use and depression.

Methods: This study was tested in the National Longitudinal Survey of Youth, a nationally representative longitudinal study of fifteen years. Data from 1984 and 1992 were used and analyzed using parametric and nonparametric bivariate analysis, and multi-variate regression.

Results: Among 12,011 youth surveyed, 36% (n=4351) were frequent marijuana users. Of frequent marijuana users, 52% reported depressed on the Center for Epidemiologic Studies Depression scale (CES-D), compared to 48% of rare or never users of marijuana ($p = 0.05$). 54% of frequent marijuana users reported "could not get going", an indicator of depression on the CES-D, compared to 49% of rare or never users ($p = .003$). Frequent marijuana users were more likely to be male (61%), and less likely to be black (21%) or Hispanic (13%).

Discussion: Frequent marijuana use predicts depression even after controlling for potential confounders. It also predicts the response of "could not get going", attributed to long-term marijuana use in previous studies. It is possible that this association was confounded and that depression preceded frequent marijuana use, but it may also suggest a causal relationship, explained by marijuana's influence on the brain's response to dopamine. As marijuana for recreational use is increasingly receiving legalization nationwide, it is important to understand its influence on mental health and long-term adverse health effects.

Felix Ho

Advisor(s): Thomas McIntyre

Disparities in treatment of biliary disease at an urban safety-net hospital

Although current guidelines recommend laparoscopic cholecystectomy as definitive treatment for a number of benign biliary diseases, studies have suggested that patient payer status and racial differences may account for disparities in treatment for benign biliary disease, resulting in lower rates of laparoscopic cholecystectomy and increased non-operative management. However, all of these studies were conducted using large national databases, and did not elucidate the causes or implications.

We conducted a retrospective chart review of 130 consecutive patients who received cholecystectomy for benign biliary disease at Kings County Hospital Center to characterize the management of benign biliary disease in a population at high risk for disparities in care.

We recorded demographic data, time from initial presentation with biliary disease to surgery, number of ED visits, number of inpatient admissions, and length of stay post surgery and in total.

At our urban public hospital, over 75% of our patients had Medicaid or were uninsured. Over 96% were black or Hispanic. All patients underwent laparoscopic cholecystectomy, with a 2.3% rate of conversion to open procedure. 54.6% of patients had an outpatient procedure. The average number of ED visits for all diagnoses was 1.57 and 38% of patients made repeat visits. Average time from initial presentation to surgery for all diagnoses was 188.8 days. Patients spent an average of 4.85 days as inpatients for all admissions for treatment of benign biliary disease.

We found that there is a delay in patients receiving cholecystectomy as definitive treatment for benign biliary disease as reflected by a long time lapse between diagnosis and surgery, a significant number of repeat ED visits and a high cumulative number of days spent in the hospital. Further research is warranted to directly address the magnitude of this disparity and develop interventions to reduce it.

Roger Cui

Advisor(s): Thomas McIntyre
Melissa Wong

Presentation of Rectal Adenocarcinoma at an Urban Public Hospital

Purpose: To characterize the presentation of rectal adenocarcinoma at a large urban public hospital that serves a predominately low-income and minority population.

Methods: This retrospective chart review evaluated all cases of rectal adenocarcinoma diagnosed at Kings County Hospital from January 2002 to October 2012. Data on demographic, geographic, pathologic and clinical variables were collected and compared with national statistics from the Surveillance Epidemiology and End Results (SEER) database by chi-square test and t-test as appropriate.

Results: Ninety-two patients diagnosed with rectal adenocarcinoma were identified. Patients were predominately African-American (84%), and the race-specific mean per capita income of the represented patient by census tract was \$19,195. The mean age at diagnosis was 61.5 years. When subdivided by decade and compared to the SEER database, more of our patients presented between 50-59 years of age (38.0% v. 22.8%, $p = 0.0005$), and fewer after 80 years of age (7.6% v. 17.0%, $p = 0.01$). 82.1% of patients presented with bleeding or anemia and only 9.5% presented after screening colonoscopy. Fewer patients presented with AJCC stage 1 disease (8.1% vs 31.3%, $p < 0.001$), and more presented with stage 4 disease (33.9% vs 17.8%, $p = 0.001$) compared to nationwide SEER data.

Conclusions: Rectal adenocarcinoma patients at our urban public hospital present at younger age and later stage than the national average. These findings suggest a role for initiating screening at a younger age in this population.

Shahnaz Miri

Advisor(s): Ivan Bodis-Wollner

Diagnosis of Parkinson Disease using visual function testing and retinal imaging

Background: Impaired vision and remodeled foveal pit are demonstrated in Parkinson's disease (PD) patients. Visual evoked potentials (VEPs) reflect abnormality anywhere in the retina to cortex pathways. We evaluated the correlation between the VEP, contrast sensitivity (CS) and foveal thickness in PD and assessed diagnostic yield of their combination.

Methods: Ten PD (20 eyes) and eight healthy subjects (16 eyes) matched for age, gender and ethnicity were enrolled in the study. All subjects underwent standard neurological and ophthalmological examination to exclude any pathology. CS was evaluated using Pelli-Robson chart. Two-channel VEP was recorded on each subject with two different stimuli (pattern reversal, frequency of 2.3 cpd; and on/off pattern frequency of 4.6 cpd). Macular optical coherence tomography (OCT) was performed using Zeiss- HD OCT and macular thickness, volume and ganglion cell-inner plexiform layer (GCL-IPL) thickness were extracted. Statistical analysis was performed using SPSS software (version 21.0).

Results: PD patients had a significantly longer N70 (reversal pattern) and P100 (on/off pattern) latency (86.7 ± 10.2 and 132.9 ± 8.7 ms, respectively) compared to healthy controls (78.8 ± 6.6 and 125.5 ± 11.5 ms, respectively) ($P=0.01$ and $P=0.03$). CS score was significantly lower in PD patients (1.66 ± 0.21 vs. 1.89 ± 0.15 ; $P=0.001$). PD patients had decreased thickness at the distance of 1.5-2.5 mm from the foveola (perifovea) ($255.0 \pm 6.5 \mu$ vs. $264.9 \pm 18.7 \mu$; $P=0.03$). N70 latency was negatively correlated with CS ($R=-0.419$, $P=0.01$) and average GCL-IPL thickness ($R=-0.529$, $P=0.001$). CS was positively correlated with parafoveal thickness ($R=0.490$, $P=0.002$). A combination of parafoveal thickness and CS score yielded an AUC of 0.784, which increased to 0.844 when combined with N70 and P100 measures.

Conclusion: Visual function is correlated with foveal morphology. A combination of VEP parameters, CS score, and foveal thickness has a high diagnostic yield for PD.

Eleanor Feldman

Advisor(s): Orit Markowitz
Daniel Siegel

Field Cancerization using Optical Coherence Tomography and Handheld Confocal Microscopy pre- and post- topical treatment.

Optical coherence tomography (OCT) and reflectance confocal microscopy (RCM) are non-invasive imaging tools that enable deeper skin visualization. Field cancerization is described as a biological process in which large areas of cells at a tissue surface or within an organ are affected by carcinogenic alterations. The process arises from exposure to an injurious environment, often over a lengthy period. Field therapy treats not only the individual cancer but all of the surrounding damaged cells that could lead to further cancers and or recurrence.

This study seeks to find evidence for field cancerization with the use of fourier domain optical coherence tomography and the handheld confocal microscope on actinically damaged skin of the face. 30 patients with a minimum of 7 non-hyperkeratotic actinic keratoses were recruited. A total of 3 actinic keratoses along with adjacent subclinical skin were scanned in both a 25cm² treated and non-treated area. A biopsy of an additional clinically suspicious actinic keratosis and its adjacent normal appearing skin was biopsied and blindly compared to both a handheld confocal scan as well as an OCT scan.

The accuracy of the devices for diagnosis was determined with H & E as the gold standard. 75% of normal appearing adjacent skin showed a biopsy result of actinic keratosis.

Optical coherence tomography had 100% accuracy with the clinical biopsy and 80% accuracy with normal appearing skin (sub-clinical) lesions. Clearance rates were determined using OCT and clinical examination. Patient results were divided based on their reaction score according to a standard reaction score scale.

Additionally, quality of life questionnaires (skindex-16) were given to all participants at baseline and at day 60. Patients had statistically significant improvement in their quality of life score. This is in contrast to previous studies that summarized decreased quality of life findings with skindex-16 after other topical field therapies.

Joshua Waxenbaum

Advisor(s): Laura Geer

Birth Outcomes Assessment from Fetal Exposure to Environmental Parabens and Antimicrobials in an Urban Immigrant Population in Brooklyn, New York

Background: Previous studies have reported detrimental effects of paraben, triclosan and triclocarban compounds. Parabens (PB) are a series of phenolic compounds that serve as preservatives in cosmetics, pharmaceuticals and food additives. Triclosan (TCS) and triclocarban (TCC) are commonly utilized for their antibacterial and antifungal properties in personal care, household and industrial products.

Objective: We examined the relationship between maternal exposure to various environmental phenols and antimicrobial compounds, and parameters indicative of infant health including weight, body length and head size at birth.

Methods: Maternal urinary concentrations of methyl-, ethyl-, propyl-, butyl- and benzylparaben, as well as TCS and TCC, were measured for each of the 190 mother-neonate pairs. Random “spot” urine specimens (n = 181) were provided once per participant during the 6th to 9th month of pregnancy. Umbilical cord blood specimens were collected from a subset of patients at the time of delivery for subsequent lab analysis (n = 38). A questionnaire was developed to ascertain history and background data. Growth parameters such as body length and head circumference were recorded for neonates at birth.

Results: In correlation analyses, we explored the relationship between biomarker levels and birth outcomes. 3'-OH-TCC and 3'-Cl-TCC were significantly, weakly positively correlated with head circumference, while MePB was correlated with length at birth. In bivariate logistic regression, TCS, 3'-OH-TCC and 3'-Cl-TCC were associated with decreased odds for low birth weight, while BuPB was associated with increased odds for low birth weight and preterm birth.

Conclusions: Our data suggest a positive association between environmental parabens and antimicrobial compounds, and negative birth outcomes. Further study is needed to explore the causality of these findings and substantiate and reproduce similar results in larger studies.

Allison Grossman

Advisor(s): Janet Rosenbaum
Howard Crystal

Using matched sampling methods to evaluate whether a mu opiate receptor polymorphism is associated with drug use in African-American women

Past research has found that a C17T polymorphism in the mu opiate receptor predicts substance abuse. One recent study using data from the Women's Interagency HIV Study used multivariate regression to reduce confounding; it found a relationship between the TT genotype and Kreek- McHugh-Schluger-Kellogg (KMSK) scores for alcohol, tobacco, cocaine, and opiate use. Regression leaves residual confounding where assumptions are not satisfied; preprocessing data with matched sampling before regression analyses can reduce confounding more than regression alone. We re-examined the same hypothesis in the same data using full matching on potential confounders of the relationship between the TT genotype and substance use that are unlikely to be intermediate variables: HIV status, age, educational attainment, and annual income. We used full matching prior to ordered logistic regression, which can minimize confounding and preserve sample size better than propensity score matching. Prior to full matching, our analysis replicated the previous study: compared with the CC/CT genotypes, the TT genotype predicted higher alcohol, tobacco, and cocaine KMSK scores and marginally predicted higher opiate scores. After full matching, the TT genotype predicted higher scores for tobacco (odds ratio [OR] = 2.02, 95% confidence interval [CI]: 1.08, 3.80) and marginally predicted higher alcohol score (OR = 1.83, 95% CI: 0.97, 3.45), but not cocaine (OR = 1.33, 95% CI: 0.70, 2.56) or opiate (OR = 1.05, 95% CI: 0.50, 2.20) scores. Analyses of rare genetic predictors of substance use should consider statistical methods to reduce confounding, such as matched sampling, rather than standard regression analyses.

Malik Johnson

Advisor(s): Mary Valmont
MaryAnn Banerji

The Effect of Decreased HbA1c Levels on the Weight of Newly Diagnosed Diabetics

Background: Previous research of Dr. Banerji revealed that some of the diabetic patients experienced an event known as near-normoglycaemic remission, in which patients showed little to no symptoms of diabetes. They were given a strict health regimen which comprised of oral medication, exercise, and a healthy diet. Many of the patients who had entered remission reportedly lowered their HbA1c (sugar) levels and their BMI.

Objective: To determine if newly diagnosed diabetic patients who experienced near-normoglycaemic remission show greater weight loss than patients who did not show remission.

Methods: We collaborated with Dr. Banerji and after gaining IRB approval were given access to her research. We reviewed 50 of her patients' files to conduct our data analysis. Our data analysis included a paired Student's test which compared pre- and post-HbA1c Levels and an independent samples Student's t-test was also conducted to compare remission and Δ BMI. SPSS was used for the data analysis and the graphs were constructed using Microsoft Excel.

Results: Twenty-one of 50 patients experienced remission. For this group, the average HbA1c Level decreased from 11.71% to 8.33%. The BMI increased, on average, from 29.93 to 30.5. Among the 39 patients who did not experience remission, there was an average gain in BMI of 0.87. There was no correlation between those who experienced remission and their change in BMI.

Conclusions: BMI is not a factor of people who go into near-normoglycaemic remission. BMI significantly increased at Time 2 while HbA1c significantly decreased at Time 2. Future research should sample a larger group of patients to explore if the original remission findings are supported.

Aija Jones

Advisor(s): Mary Valmont
Daniel Cukor

The Effects of Anxiety and Depression on Medication Adherence in ESRD Patients

Introduction: The National Health and Nutrition Examination survey (NHANES) reports that 16.8% of the United States population above the age of 20 has ESRD. Men are at higher risk of getting ESRD than women, and, in terms of ethnicity/race, African Americans and Hispanics have the highest ESRD incidence rate. Studies show that mental health conditions can have adverse effects on health, with 33% of dialysis patients deaths linked to anxiety or depression.

Objective: To determine if mental health conditions such as anxiety and depression are barriers to medication adherence in ESRD patients.

Methodology: The data was previously collected from the ESRD patients in the SUNY Downstate Parkside Dialysis Clinic as part of a larger study. The data was gathered from a population of African American/Afro-Caribbean patients. The independent variables depression and anxiety were measured by the Becks Depression Inventory (BDI), and the State Trait Anxiety Inventory (STAI). Medication adherence was measured by the Medication Adherence Reasons Scale (MARS).

Results: The ESRD-AQ Behavior (p-value 0.33) did not support our hypothesis while the ESRD-AQ (p-value 0.113) did support our statistically significant. The MARS (p-value 0.419) did not show any statistical difference between the groups, not supporting our hypothesis. The ITAS-M (p value 0.117) did support our hypothesis, but it was not statistically significant.

Conclusion: Our study population showed that patients with either depression or anxiety are at greater risk of poor adherence. The ITAS supported the hypothesis, but it was not significant. Future research should focus on whether early detection and treatment of anxiety and depression would limit negative outcomes for depression in dialysis patients.

Jean Poulard

Advisor(s): Mary Valmont
Michael Joseph, Tracey Wilson, Yolene Gousse

Attitudes Towards Health and the Effect on HIV Testing in Heterosexual African American Males

Background: HIV is a growing issue in the United States with more than 25% of new HIV cases occurring through heterosexual sex. In 2010, less than half of the population who had multiple sex partners used a condom. Approximately 44% of new HIV cases were African Americans. Within the Flatbush area, it has been reported that less than 1 in 3 individuals have been tested for HIV. Given this data, there is a need for more research in order to increase testing in a majority African American community who are disproportionately affected by HIV.

Objective: Determine whether the perception of one's health is associated with getting tested for HIV, among heterosexual African American males of Brooklyn, New York.

Methods: This study was conducted in barbershops, where recruiters approached customers and attempted to have them to take a survey. The data was analyzed with the use of the Chi Square, two by two tables, and odds ratios in order to assess the strength of the relationship between the independent and dependent variables.

Results: HIV testing (26/80) (74/80). Education status [$\chi^2=0.81$, $p=0.36$ OR=1.86, 95% CI (0.50, 8.91)]. Health insurance status [$\chi^2=0.94$, $p=0.33$, OR= 1.41, 95% CI (0.58, 4.58)]. My own health is important to my community [$\chi^2=0.20$, $p= 0.65$, OR=0 .73, 95% CI (0.15, 2.81)]. I Can Make a Difference in my Community [$\chi^2= 0.37$, $p=0.55$ OR=1.41, 95% CI (0.43, 4.37)]

Conclusions: There was no significant association between the participants' attitudes toward health and getting tested for HIV. Further investigation with a larger sample size is needed to find stronger results. Insurance coverage is not a significant factor in getting tested for HIV.

Momina Tariq

Advisor(s): Mary Valmont
Suzanne Burke-McGovern, Rauno Joks

Effects of Asthma Medication Adherence on Symptom Control in a Predominately Black Pediatric Population

Background: Asthma is a chronic respiratory condition marked by constrictions of the bronchi in the lungs. Symptoms include wheezing and coughing. Non-adherence to medication may contribute to morbidity and mortality in pediatric asthma patients. Adherence to asthma medication regimens tends to be poor in the USA mainly in the African American communities; with reported rates of non-adherence ranging from 30% to 70 % (Global Initiative for Asthma, 2012). Incidence of asthma in African American children is 16.4% higher compared to Caucasians (Health 2012-2013). African American children have a 70% higher incidence rate than Caucasian children (Health 2012-2013).

Objective: This study seeks to determine whether barriers to asthma medication adherence such as financial burden, perception of medication importance, and concerns of side effects affect asthma control.

Method: Participants were pediatric African Americans from the SUNY Downstate Pediatric Primary Care Practice. The Asthma Control (ACT) and Adherence Estimator (AdEst) were used to measure asthma control. Barriers were measured by the Merck Adherence Estimator and the Asthma Control Test.

Results: Four graphs were plotted: concern, commitment, cost, and composite adherence vs. control. The mean score on the ACT was 20.6 and the mean score on the AdEst was 4. There was a weak relationship due to the R-values of the four graphs. There were negative correlations between Commitment vs. Control and the Composite vs. Control. There were positive correlations between Concern vs. Control and Cost vs. Control.

Conclusion: Patients' commitment to medication regimens affects asthma severity. Patients with high AdEst scores, concern about medication harm and commitment had low ACT scores, demonstrating poor asthma control. Identifying and addressing factors that affect medication adherence and the effect that they have on asthma control can help clinicians design interventions to overcome barriers to adherence.

Mary Valmont

Advisor(s): Michael Joseph
Tracey Wilson, Yolene Gousse

Attitudes Towards Health and the Effect on HIV Testing in Heterosexual African American Males

Background: HIV is a growing issue in the United States with more than 25% of new HIV cases occurring through heterosexual sex. In 2010, less than half of the population who had multiple sex partners used a condom. Approximately 44% of new HIV cases were African Americans. Within the Flatbush area, it has been reported that less than 1 in 3 individuals have been tested for HIV. Given this data, there is a need for more research in order to increase testing in a majority African American community who are disproportionately affected by HIV.

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Conclusions: There was no significant association between the participants' attitudes toward health and getting tested for HIV. Further investigation with a larger sample size is needed to find stronger results. Insurance coverage is not a significant factor in getting tested for HIV.

Anupriya Gogne

Advisor(s): Chella Kamarajan

Reduced auditory P3 amplitude in adolescents at high risk for alcoholism

Objective: Alcoholism has been considered to be part of a spectrum of disinhibitory disorders, with impulsivity being an important characteristic. Event-related potentials (ERPs) have been used as effective tools to study cognitive deficits related to alcoholism and risk. Previous studies reported low P3 amplitudes of the ERP and high impulsivity in alcoholics. Our objective in this study was to investigate the P3 amplitude as well as impulsivity in high risk subjects with a heavy loading of family history of alcoholism using an auditory oddball (AOD) paradigm. Current source density (CSD) was computed in each group to examine brain topography of P3. Methods: Offspring in an adolescent age range (12-17 years) from HR families (N=396) from the multi-site Collaborative Study on the Genetics of Alcoholism (COGA) and offspring from low risk (LR) control families (N=79) were assessed with the AOD paradigm; P3 amplitudes to target stimuli were measured at midline frontal (Fz), central (Cz), parietal (Pz) and occipital (Oz) regions. Barratt Impulsiveness Scale (BIS) was used to evaluate impulsivity in both groups. Subjects were further grouped for gender within this age group. Results: HR subjects in both gender groups showed statistically significant lower P3 amplitudes in the posterior region ($p=0.007$) than LR subjects. Further, HR subjects showed higher impulsivity in motor, attentional, and total BIS scores in both gender groups. HR and LR subjects manifested differences in both intensity and topography of CSD activation. The differences in CSD activation across risk groups were stronger in males as compared to females. Conclusions: Our results demonstrate significant cognitive deficits as reflected by lower P3 amplitudes and differential CSD profiles in subjects from HR COGA families. Higher impulsivity in HR subjects further establishes the view that impulsivity and/or underlying neurocognitive disinhibition may contribute to vulnerability to develop alcoholism.

Glenford Robinson

Advisor(s): Günter Blobel
Ivo Melčák, Alok Sharma

Biophysical characterization of Nup62 and its complexes: A reductionist approach towards IBSN

Nuclear Pore Complexes (NPCs) are the largest known macromolecular structures that traverse the inner and outer nuclear membranes. They facilitate nucleocytoplasmic transport of large ribonucleoproteins. The central channel of the NPC is made up of three nups: Nup58, Nup54, and Nup62, collectively referred to as “channel nups.” Nup62 interacts with Nup54 through an alpha helical domain. A missense mutation in this domain is associated with autosomal recessive infantile bilateral striatal necrosis (IBSN). The project was aimed to express and purify either the wild-type or Q391P mutated Nup62 in complex with Nup54 or Nup88. We were able to express and purify the wild-type and Q394P mutated Nup62L alone and in complex with Nup54. Thus, in agreement to what has been earlier reported for shorter constructs of Nup54·Nup62, the longer constructs, used in this study, also suggest that the Q391P mutation destabilizes the complex.

Brian Albertson

Advisor(s): Jason Lazar
Louis Saliccioli

Cerebrovascular Reactivity, Arterial Stiffness and Vasculopathy In Adult Patients With Sickle Cell Anemia

Sickle cell anemia (SSA) is a common inherited hemoglobinopathy which results in a vasculopathy. The inter-relationships of vascular structure and function in this population are not well characterized. Study objectives were to characterize cerebrovascular vascular reactivity (CVR), arterial stiffness and carotid intimal medial thickness (CIMT) in adult SSA.

Middle cerebral artery CVR was assessed using the breathholding index (BHI), obtained by measuring changes in transcranial Doppler velocities with permissive hypercapnea induced by passive breath holding. Lower BHI indicates reduced CVR. The heart rate corrected augmentation index (AI) and carotid-radial pulse wave velocity (PWV) were assessed by applanation tonometry. CIMT was obtained with high-resolution ultrasound. We compared 37 adult SSA patients (age 43±12yrs; 70% female) with 25 age and gender matched normal controls (NLS).

Mean arterial pressure was lower in SSA compared to NLS (80±mmHg vs. 87±9mmHg, $p = 0.003$). On CVR testing, BHI responses were lower in SSA compared to NLS (0.21±0.6 vs. 0.93±0.8, $p = 0.001$). CIMT was greater (0.64±0.11 cm vs. 0.53±0.09 cm, $p < 0.000$) and AI was higher (22±16% vs. 13.2±14%, $p = 0.03$) in the SSA group. There was a trend towards lower PWV in SSA (7.7±1.4 vs 8.3±1.1 m/s, $p = 0.1$). CVR correlated inversely with CIMT ($r = -0.33$, $p = 0.01$) and with AI ($r = -0.28$, $p = 0.03$). On multivariate analysis (with AI, CIMT and SSA), SSA was the only predictor of BHI ($B = -0.52$, $p = 0.04$).

In summary, SSA patients have impaired CVR, increased CIMT, higher AI and a trend toward lower PWV than NLS. SSA patients exhibit a unique profile of vascular abnormalities including lower mean arterial pressure, increased wave reflection and CIMT and possibly lower PWV. These abnormalities may reflect higher intravascular volume in the setting of arterial vasodilation and arterial wall thickening.

Sriya Avadhani

Advisor(s): Jason Lazar
Louis Saliccioli

Comparison of Lower Body Weight Support on Ejection Duration in Healthy Subjects and Patients with Heart Failure

Despite advancements in cardiac imaging, there are pitfalls in assessment of left ventricular (LV) contractility. Noninvasive measures such as ejection fraction (EF) and stroke volume are load dependent. The gold standard, end-systolic pressure volume relation requires catheterization with high-fidelity catheters and preload reduction with a balloon catheter placed in the inferior vena cava. Lower extremity positive pressure (LEPP) treadmills are used for rehabilitation and may benefit patients with heart failure (HF). LEPP treadmills lower musculoskeletal strain, compress the lower body and increase intrathoracic volume. Applanation tonometry is a noninvasive method that provides recordings of the aortic waveform from which systolic ejection duration (ED), a measure of systolic performance, is measured. We studied effects on ED during progressive LEPP reduction of 25%, 50%, and 75% of body weight in 25 healthy male subjects (N) and 26 patients with HF (age 32±8 vs 64±9; $p < .001$). LEPP decreased heart rate (HR) to a greater extent in N vs HF (10 ± 12 vs 4 ± 13 bpm; $p < .001$). Peripheral and central blood pressures remained unchanged in both groups ($p = \text{NS}$ for all). The ED was slightly higher at baseline in N vs HF (256 ± 21 vs 249 ± 25 ms; $p = .31$). Both the N and HF groups increased ED with increasing LEPP with less increase in the HF group (15% and 11% respectively). On repeated measures analyses the groups exhibited different ED responses before and after adjusting for HR, systolic BP and age ($p = .02$). The ED curves may represent the Frank-Starling relationship, which relates LV filling pressure/preload to LV work resulting in a curvilinear function that plateaus at higher filling pressures. In conclusion, progressive LEPP decreases HR and increases ED in a step-wise manner. The changes are less marked in HF compared to N. The combination of LEPP and applanation tonometry measured ED may allow assessment of contractile reserve with varying preload.

Muhammad Ihsan

Advisor(s): Jason Lazar
Louis Saliccioli

Comparison of the Timing of the Korotkoff Sounds in the Lower and Upper Extremity

Increased arterial stiffness is an early step in the development of cardiovascular (CV) disease. The timing of Korotkoff Sounds (KS) during blood pressure (BP) measurement may reflect arterial properties. Our objectives were to determine the feasibility of recording KS from the lower extremities using an electronic stethoscope and to determine the optimal level of cuff inflation pressure. KS were recorded over the brachial (BA) and pedal arteries (PA) in 55 healthy subjects with simultaneous ECG for 60 seconds at diastolic BP (DBP), DBP+10mmHg, DBP+20mmHg, and DBP+30mmHg. The time from the QRS R wave to the KS waveform (QKD interval) was determined. QKD velocity (v) was calculated as distance the pressure wave traveled from heart to arterial site /QKD. Carotid BA and carotid PA pulse wave velocities (PWV) were obtained by applanation tonometry. Adequate QKD recordings were obtained in 96% at DBP and in 100% at higher pressures from the BA and in 70% to 89% of subjects from the PA (maximal yield at DBP+20mmHg). QKD v was higher at the PA than the BA at each pressure. QKD v decreased more markedly at the BA (17%) than PA (8%) with increasing cuff pressures. On multivariate analyses, QKD was independently associated with height and pulse pressure at the BA and with height and age at the PA. PA QKD v values correlated with carotid-pedal PWV ($r = .51$, $p = .001$), whereas BA QKD v and carotid brachial PWV did not ($r = .12$, $p = .44$). QKD is measured at the PA and BA sites with the highest yield at DBP+20mmHg and are correlated ($r = .48$, $p < .001$). In conclusion, while the BA provided a greater yield of adequate recordings, PA QKD values were correlated to age, whereas BA QKD were not. PA QKD v values more closely correlate with PWV and are less susceptible to variations in occlusion pressures. Technical improvements may increase the yield of PA QKD and make this preferable to BA QKD. This technique may be a simple method to assess arterial stiffness.

Haroon Kamran

Advisor(s): Jason Lazar
Louis Saliccioli

Differential Assessment of Microvascular and Macrovascular Function

Endothelial dysfunction is an early step in atherosclerosis. The usual method to evaluate endothelial function is ultrasound measurement of the increase in brachial artery mean flow velocity (MFV) and dilatation (BAD) by release of upper arm cuff occlusion. Passive leg raising (PLR) is an alternative provocation that centralizes blood volume and increases cardiac output resulting in BAD without affecting the downstream microvasculature.

We studied 102 subjects with and without diabetes (DM) (42 normal, 60 DM, age 48 ± 19 yrs.). BAD and MFV were assessed with ultrasound both during hyperemia and PLR to evaluate macrovascular function. Laser Doppler Flowmetry (LDF) during both hyperemia and PLR were measured to assess microvascular function. The microvascular and macrovascular responses elicited by the two provocative maneuvers were compared using SPSS statistical software.

Among the 42 normal subjects, hyperemia increased BAD ($15.4 \pm 9.3\%$, $p < .001$), MFV ($407 \pm 301\%$, $p < .001$) and LDF ($280 \pm 286\%$, $p < .001$). PLR increased BAD ($5.4 \pm 3.9\%$, $p < .001$) and MFV ($24 \pm 48\%$, $p = .007$), but did not change LDF ($12 \pm 53\%$, $p = .49$).

Among the 60 DM subjects hyperemia increased BAD ($5.96 \pm 5.3\%$, $p < .001$), MFV (304 ± 287 , $p < .001$) and LDF ($222 \pm 345\%$, $p < .001$). PLR increased BAD ($2.1 \pm 3.2\%$, $p < .001$) and MFV ($21 \pm 70.7\%$, $p = .012$), but did not change LDF (4.6 ± 49.6 , $p = .12$). There was significant correlation between hyperemia LDF and the difference between hyperemia and PLR BAD ($r = .384$, $p < .001$). The differential effects of the 2 techniques (hyperemia-PLR) was greater for normals versus DM (10.3 ± 9.5 vs 3.9 ± 4.9 , $p < .001$). This suggests a microvascular component to hyperemia but not PLR.

In summary, The differential effect of the two techniques may be useful to distinguish and quantify microvascular dysfunction.

Arismendy Nunez

Advisor(s): Jason Lazar
Louis Saliccioli

Effects of Lower Body Weight Support on Arterial Hemodynamics and Wave Reflection in Patients with Heart Failure

Lower body weight support treadmill exercise is associated with lower musculoskeletal strain than traditional treadmill exercise and is used in patients with orthopedic and neurological conditions. Lower body weight support (WS) evokes hemodynamic changes due to mild lower extremity compression resulting in increased intrathoracic blood volume. Using radial artery applanation tonometry we previously demonstrated that normal subjects exhibit changes in arterial hemodynamic and wave reflection indices during WS. Here we study effects of WS of 25%, 50%, and 75% of body weight in 21 men (age 64 ± 9 yrs.) with systolic heart failure (EF $28 \pm 10\%$). Applying %WS in random sequence we measured resting short term changes in hemodynamics and wave reflection indices. Data were analyzed with SPSS using linear mixed modeling.

WS was not associated with changes in heart rate (75 vs. 70 bpm; $p = 0.5$), peripheral (85 vs. 85 mmHg; $p = 0.9$) or central (84 vs. 82 mmHg; $p = 0.9$) mean arterial pressures or in the pulse pressure amplification ratio, augmented pressure (4.4 to 5 mmHg; $p = 0.9$) or heart rate corrected augmentation index (13 to 14%; $p = 0.9$). Both the ejection duration (251 to 278 ms; $p = 0.03$) and systolic duration of the reflected pressure wave (104 to 130 ms; $p = 0.04$) increased step-wise from rest to peak WS. Indices of left ventricular workload and oxygen demand, the subendocardial viability ratio ($p = 0.8$) and wasted energy ($p = 0.7$), did not change with WS. In summary, in men with systolic HF, lower body WS did not alter peripheral or central arterial pressure, heart rate, reflected wave amplitude, pulse pressure amplification ratio, or wasted energy, but it did result in significant increases in ejection duration and systolic duration of the reflected wave. These findings contrast with those reported in normal subjects. The clinical implications of WS during treadmill exercise in subjects with HF merits further investigation

Jacqueline Tin

Advisor(s): Jason Lazar
Louis Saliccioli

Cognitive Function and Cerebrovascular Reactivity in Patients with Sickle Cell Anemia

Sickle cell anemia (SSA) is an inherited hemoglobinopathy associated with early cognitive decline. We hypothesized that this decline is associated with vascular dysfunction. Study objective was to evaluate the relationship between cerebrovascular reactivity (CVR) and cognitive function in SSA.

Methods

Middle cerebral artery CVR was assessed using the breath holding index (BHI), which was obtained by measuring changes in transcranial Doppler velocities with permissive hypercapnea induced by passive breath holding. Lower BHI indicates reduced CVR. Cognitive function was evaluated by using STROOP color naming (SCN), word reading duration (SWR) and interference (SIT) tests, letter number sequencing (LNS), and symbol digit modalities (SDM).

We compared 45 adult SSA patients (age 43±12yrs; 59% female) with 41 age- and gender-matched normal controls (NL).

Results: BHI correlated with LNS total ($r= 0.31$, $p=0.02$), and inversely with SCN ($r= -0.24$, $p=0.03$), SWR ($r= -0.25$, $p=0.02$), and SIT time ($r= -0.32$, $p<0.003$). BHI was not correlated with SDM. On multivariate analysis (with age, gender, education), SSA was an independent predictor of SIT time ($B = .35$, $p=0.03$) and SCN ($B = .7$, $p<0.001$), while both SSA and education were independent predictors for SWR and LNS total. On multivariate, BHI and education (age, sex, education) are independent predictors of LNS total ($B = .25$, $p=0.03$).

Conclusion: SSA is associated with impaired cognition. Reduced CVR as measured by the BHI is associated with impaired cognitive function. These findings suggest that the cognitive dysfunction in SSA patients may be associated with vascular dysfunction.

Suzanne Burke-McGovern

Advisor(s): Rauno Joks

The Effect of Educational Intervention on Adherence Estimator Scores and Asthma Control in Pediatric Patients

Rationale: Non-adherence to asthma medications is a major factor contributing to the morbidity and mortality associated with asthma in the pediatric population. We investigated whether a single asthma education session improved medication adherence and asthma control.

Methods: A cross-sectional study was conducted with outpatient pediatric patients with persistent asthma. Children and their caregivers ($n=36$) were asked to complete 2 surveys on 2 occasions separated by 2 months. These surveys consisted of the Adherence Estimator™ (AE) (Merck), a 3 question survey assessing perceived views of medication concern, commitment and cost; and the Asthma Control Test (cACT/ACT). Patients and caregivers were educated verbally within 1 hr of the initial survey. Follow-up surveys were completed by $n=20$ (55% of initial group). Data was analyzed with the Wilcoxon Signed Rank test.

Results: Pre-education the median total AE score was 4.9 and mean ACT score was 19.2 indicating a medium risk for adherence problems and well controlled asthma, respectively. Mean scores for concern, commitment and cost were 2.4, 2.4 and 0.4 respectively, indicating moderate to low risk for adherence problems. After education the mean total AE score was 3.3 ($p= 0.315$) and mean ACT score was 20.9 ($p=0.038$) indicating an overall reduced risk of medication non-adherence and significant improvement in asthma control. Mean scores for concern, commitment and cost were 1.5 ($P= 0.49$), 1.7 ($p=0.59$) and 0.1 ($p=0.25$), respectively, indicating low risk for non-adherence in all categories.

Conclusion: Educating pediatric patients and their caregivers about their asthma medications significantly improved asthma control. Although educating pediatric patients and their caregivers about their asthma medications did reduce their overall risk of non-adherence in all categories of adherence (concern, commitment and cost) these changes were not significant.

Kobkul Chotikanatis

Advisor(s): Rauno Joks

C5a Mediated Induction of Phosphorylated P38 MAPK Expression By Blood T Lymphocytes in Adults with Allergic Asthma

Background: Complement split product C5a levels increase in airways after allergen provocation in asthmatics. We reported plasma C5a levels relate to asthma severity and quality of life scores. Expression of phosphorylated p38 MAP kinase (p38 MAPK) in lymphocytes from allergic adults correlates with total serum IgE. We investigated whether C5a increases p38 MAPK by lymphocytes and its association with IgE production in vitro.

Methods: PBMCs (1.5×10^6 /mL) from allergic asthmatics (n=10, age 35-66 years) were cultured with anti-CD40 antibody and recombinant-human interleukin-4 ± recombinant-human C5a (0.1-10 µg/mL) for 2-10 days. P38 MAPK levels (% expression) by CD4+ and CD8+ T lymphocytes were determined on day 2 and 4 (flow cytometry). IgE levels in supernatants were determined on day 10 (ELISA). Serum IgE levels were determined (fluoroenzymeimmunoassay).

Results: Serum IgE levels were 1646.7 ± 1405 U/ml. C5a (1 and

10 µg/ml) significantly increased p38 MAPK levels by CD8+ T lymphocytes at 96 hours compared to without C5a ($p = 0.037$ and 0.047 , respectively). CD4+ T lymphocytes had no significant change in p38 MAPK ($p = 0.093$, $p = 0.646$). In 7/10 (70%) of subjects, IgE production increased (0.04-3.48 ng/ml, mean 2.08 ± 0.52) from baseline IgE (7.19-45.49 ng/ml, mean 10.48) when cultured with C5a. However, in vitro IgE production had no significant correlation with p38 MAPK or serum IgE levels.

Conclusion: C5a upregulates p38 MAPK by CD8+ T cells of IgE+ allergic asthmatics. CD8+ T cells with increased P38 MAPK may serve as helpers for IgE response.

Irina Katayeva

Advisor(s): Rauno Joks

Correlation of development of allergic disease to parental history of cancer in Chinese immigrant populations residing in Brooklyn

Rationale: The association of allergic disease with cancer is understudied. We investigated the relationship between development of allergic disease/asthma in adult Chinese immigrants to Brooklyn and their parental history of cancer. Methods: Retrospective survey was conducted for adult immigrants to Brooklyn from People's Republic of China (n=164) who developed allergic disease (allergic rhinoconjunctivitis, asthma, eczema, food allergies) after immigration to Brooklyn, and Chinese immigrants to Brooklyn without allergic disease (n=128). All participants completed a survey regarding history of cancer of any kind in their fathers and mothers, personal history of cancer, and development of allergic disease. Total serum IgE in subjects and controls were determined by ELISA, Fisher's exact test and Wilcoxon rank-sum 2 sided tests were used for statistical analysis. Results: There was a significant association between development of allergic disease in adult Chinese immigrants and any parental history of cancer ($p = 0.0052$); allergic disease was also associated with development of paternal cancer ($p = 0.024$). Approximately half of paternal cancers in allergic subjects were gastrointestinal solid tumors (11/21); 4 of 21 were lung cancers. Allergic disease did not associate with history of maternal cancers ($p = 0.26$). There was no correlation between personal history of malignancy (7/290) and IgE levels ($p = 0.598$). Conclusions: Parental, notably paternal, history of cancer in Chinese immigrants is associated with development of allergic disease in adult children who have immigrated to Brooklyn.

Mili Shum

Advisor(s): Rauno Joks

Allergen Specific IgE Response Is Similar in HIV-1 Seropositive and Seronegative Adults: Implications for HAART Induced Th2 to Th1 Switching

Rationale: Advanced HIV disease has been associated with Th2 mediated IgE responses, including anti-HIV IgE, and decreased atopy. The effect of HAART (highly active antiretroviral therapy) on Th2 mediated allergic IgE responses has not been determined.

Methods: Retrospective chart review was performed for adults seen in Allergy clinic at University Hospital of Brooklyn during 7/2000 to 5/2014. Subjects included HIV-1 patients on HAART and a control group consisting of HIV-1 seronegative patients (age and sex matched with a clinical visit in the same month). Total and allergen specific serum IgE was determined by ImmunoCAP assay; Skin prick test (SPT, Dermapik) for aeroallergens was performed using the Dermapik method. A mixed linear model was constructed for each dependent variable (IgE, no. of positive allergy results). Fixed factors were HIV status and gender; age was introduced as a linear covariate; matched pair ID was introduced as a random factor.

Results: Seventy-four subjects were analyzed with equal number of subjects in each group. HIV-1 seropositive subjects on HAART and controls had total serum IgE of 90.95 IU/ml and 144.54 IU/ml respectively ($p=0.23$) and similar numbers of positive allergen specific IgE responses of 3.34 and 4.06, respectively ($p=0.28$).

Conclusions: These findings suggest there is limited effect of HAART on Th2 to Th1 switching.

Thomas Duggan

Advisor(s): Jacob Aranda

Acute and Chronic Effects of Intravitreal Bevacizumab on Lung Biomarkers of Angiogenesis in the Neonatal Rat

Background: Intravitreal bevacizumab (Avastin) is an irreversible vascular endothelial growth factor (VEGF) inhibitor used off-label to treat severe retinopathy of prematurity (ROP) in extremely low gestational age neonates (ELGANs). ELGANs who are at the highest risk for developing severe ROP often experience episodes of hypoxia, or intermittent hypoxia (IH) during oxygen therapy. The effects of permanent VEGF inhibition on the development of the preterm lungs is unknown as there are no long-term studies.

Objective: We examined the hypothesis that Avastin leaks into the systemic circulation during exposure to intermittent hypoxia (IH) and has adverse effects on pulmonary microvascular maturation, leading to pulmonary hemorrhage and long-term pulmonary sequelae.

Methods: Neonatal rats at birth were exposed to either: 1) hyperoxia (50% O₂); 2) IH (50% O₂ with brief episodes of 12% O₂) from P0-P14. Room air littermates served as controls. At P14, a single dose of Avastin (0.25 mg in 0.01 mL) was injected into the vitreous cavity of the left eyes; a control group received equivalent volume saline. At P23 and P45 lung biomarkers of angiogenesis (HIF1 α , VEGF, sVEGFR-1, IGF-I, NO_x) were examined. **Results:** One week post Avastin treatment (P23) lung VEGF, NO_x and HIF1 α were increased with hyperoxia and IH while sVEGFR-1 levels were lower. IGF-I remained unchanged. At P45, lungs from animals exposed to IH and treated with Avastin were severely hemorrhagic. This was associated with higher VEGF and NO_x levels, and lower IGF-I and sVEGFR-1. HIF1 α was higher only in the Avastin-treated hyperoxia group. **Conclusions:** Intravitreal Avastin penetrates the blood-ocular barrier, enters the systemic circulation and alters lung biomarkers of angiogenesis. Avastin suppression of sVEGFR-1 (the endogenous VEGF regulator) may be responsible for the higher VEGF levels which could lead to increased pulmonary hemorrhage. Caution for the uncontrolled use of Avastin in ROP is warranted.

Genevieve Gabriel

Advisor(s): Geetha Chari

Anti-N-Methyl-D-Aspartate Receptor (NMDAR) encephalitis: A Case of Rapid Developmental Regression in a Toddler

Anti N-methyl-D-aspartate receptor (NMDAR) encephalitis in children is known to present with psychiatric symptoms, seizures and dyskinesias. We present a case of rapid developmental regression in a child due to anti-NMDAR encephalitis. A 46-month old boy presented with multifocal seizures and developmental regression following a tonsillectomy and adenoidectomy. Within a month, he had lost all expressive language and had significantly impaired receptive language. He also lost fine motor skills. However, he did not display any oro-facial dyskinesias which are commonly described in this condition. Continuous electroencephalogram was abnormal and showed slow background, multifocal epileptiform discharges and electrographic seizures. The EEG findings which were characteristic of Anti-NMDAR encephalitis as has been described in pediatric patients in the literature. He was treated with intravenous immunoglobulin and steroids. Anti-NMDAR antibodies were detected in the boy's cerebrospinal fluid as well as serum. One month after treatment, his language and motor skills had returned to baseline. He did not require second-line treatment. Our case exemplifies the importance of suspecting anti-NMDAR encephalitis as the cause of rapid developmental regression.

Ammar Mahmoud

Advisor(s): Ozgul Muneyyirci-Delale

Link Between Thyroid Disorder and HPV

In regards to cervical HPV infection, it has been well documented that multiple risk factors exist and are associated with increase of likelihood of infection persistence and progression. It is hypothesized that abnormalities in thyroid function could have effects on cellular immunity and ability to abate neoplastic progression and resolve cervical HPV infection. A recent survey performed by SUNY Downstate OBGYN department looked at the incidence and possible association of cervical HPV infection and abnormalities of thyroid function. A survey of 134 women of reproductive age was collected. Results displayed an association of thyroid dysfunction with increased HPV prevalence, $P=0.11$. Intent to further enhance study size is currently underway.

Anant Dixit

Advisor(s): Aditya Maheshwari

Bidirectional Barbed Sutures in Total Joint Arthroplasty: What is the Evidence? A Systematic Review and Meta-Analysis

Purpose: Newer methods of wound closure such as bidirectional barbed sutures hold the potential to decrease closure time and thus overall operating room costs during total joint arthroplasty (TJA). However, it is unclear whether these sutures have similar clinical outcomes or whether they place the patient at a risk for developing wound complications, which may potentially outweigh the time saving benefits of these sutures.

Methods: A systematic review of the literature was performed to identify all studies that reported the use of a bidirectional barbed suture during TJA. Studies that were either level I or II were included in a mixed-effects meta-analysis model which compared outcomes between barbed and standard sutures while the remaining (level III and lower) were included in a systematic review. The mean major and minor complication rate was determined as well as the amount of time saved and when possible the overall cost savings (or loss) associated with the suture.

Results: Six level I studies were identified; however, only two were related to total joint arthroplasty. Evaluation of non-randomized trials resulted in two level III studies, one level IV study, and one biomechanical study. Results of the meta-analysis demonstrated that barbed sutures did not have significantly higher odds for either a minor (OR: 1.01, 95% CI: 0.30 – 3.4) or major complications (OR: 1.29, 95% CI: 0.16 – 10.3). Wound closure time decreased by a mean of 10.5 ± 1.1 min, which corresponded to a total cost savings of $\$509.64 \pm 129.74$.

Conclusion: Bidirectional barbed sutures are consistently associated with shorter wound closure time in randomized controlled trials. This corresponds to cost savings even when the higher cost of these sutures is accounted for. The odds of having either a minor and major complication was not significantly different from patients who were closed using standard sutures. Current evidence supports continued use of bidirectional barbed sutures.

Joseph Munn

Advisor(s): Aditya Maheshwari

Is There a Difference Between Limb Salvage Versus Limb Amputation in Conventional Appendicular Osteosarcoma? A Systematic Review of the Literature

Purpose: Osteosarcoma is the most common primary bone sarcoma. Clinical questions we evaluated in this systematic review were: prognostic factors, disease free and overall survival, recurrence and metastasis, and complications of surgery. In an attempt to provide a more homogeneous discussion, we will primarily focus on appendicular osteosarcoma in general.

Methods: We evaluated peer-reviewed literature by searching the electronic medical databases Pubmed, Medline, Embase, and Scopus from 1980 to 2014. The 51 articles included studies with the following level of evidence: Level II (1), Level III (27), Level IV (19), and Level V review papers (4).

Results: Prognostic Factors included: Response to chemotherapy, surgical margins achieved, tumor location and size, extent of surgery, gender, axial tumor location, male gender, history of symptoms longer than 2 months, age, and histological subtype.

Disease Free and Overall Survival: There has been a steady rise in disease free and overall survival for patients who have osteosarcoma, primarily due to advancements in diagnostic and therapeutic measures, such as imaging, chemotherapeutic agents, surgical techniques, and prostheses design.

In the present systematic review, we observed that the mean survival rate for salvage was 62% (range, 41-84%, STDev 21.5) and for amputation was 58% (range, 49-74%, STDev 11.8).

Recurrence and Metastasis: It has been demonstrated by various studies that there is no significant difference in recurrence or metastasis between salvage or amputation procedures.

Complications of Surgery: The complication rates vary across the literature and range from 0-70%.

Conclusion: Limb salvage and amputation are both viable treatment options for patients who have osteosarcoma. These procedures having almost equivalent recurrence and survival rates. However, the better cosmetic perception of limb salvage makes it the currently preferred choice for most patients and surgeons, if technically possible.

Qais Naziri

Advisor(s): Aditya Maheshwari

HIV Markers and Post-Operative Infection Following Total Hip Arthroplasty

Purpose: As demand for total hip arthroplasty (THA) in Human Immunodeficiency Virus (HIV)+ patients grows, it is valuable to identify predictive markers of post-operative complication among these high-risk surgical candidates. The purpose of this study was to assess the utility of preoperative CD4+ counts and viral loads in HIV+ patients to determine the risk for post-operative infection.

Methods: Medical records were retrospectively reviewed for 20 HIV+ patients who underwent THA. We extracted data on patient demographics (age, race, gender, BMI), pre-operative serum HIV markers (CD4+ count, HIV viral load), and post-operative deep wound infection (no, yes), as defined by the Centers for Disease Control and Prevention. We defined a patient's HIV infection status as "high risk" if their pre-operative CD4+ count was ≤ 350 cells/mm³ and/or their HIV viral load was detectable (>50 copies/mL), as stated in the US Department of Health and Human Services (HHS) guidelines. Descriptive statistics and Chi-Squared tests were calculated using SPSS version 22.

Results: The cohort consisted of 12 men and 8 women. We identified 10 (50%) "high risk" patients. Risk of post-operative wound infection was identical (10%) in both groups.

Conclusion: Although our numbers are limited, pre-operative serum markers of HIV infection (CD4+ count and HIV viral load) may have limited value in predicting post-operative wound infections. Orthopaedic surgeons should take standard precautions against post-operative wound infection in HIV-positive patients undergoing THA, regardless of the severity of infection. Future studies are needed to further elucidate the role of CD4+ count and viral load as predictors of postoperative infection risk.

Kemjika Onuoha

Advisor(s): Aditya Maheshwari

Reconstruction Plate-Based Antibiotic Cement Spacers: Clinical Outcomes and Description of Technique

Purpose: In the setting of chronic deep periprosthetic hip infection the current standard of care is a two-stage exchange with placement of a temporary antibiotic cement spacer and treatment with intravenous antibiotics. Several options for cement spacers exist, including commercially available spacers. However, these may lead to higher costs. We report on a novel antibiotic spacer, which may potentially be a less-expensive alternative.

Methods: We reviewed medical records of patients treated for a deep periprosthetic hip infection following THA between 2004 and 2012. Antibiotic spacers were constructed from a 12 to 16 hole recon plate which was bent to provide adequate soft tissue tension (mean, 125°) and a cement ball was created that matched the acetabulum. Biomechanical failure was defined as fracture of the plate/dissociation of the cement head from the plate and clinical failure as failure to control infection. Cost was compared to commercial cement spacers.

Results: In total 13 males and 8 females with a mean age of 68.9 years (range, 44-92) and mean BMI of 26.4 (range 18.8-31.9) received 24 spacers. Plate lengths were six 12-hole, three 14-hole, and eight 16-hole, as well as seven premade spacers. The mean time between spacer placement and reimplantation was 6.4 months (range, 1.8-18). At reimplantation, none of the 17 handmade spacers failed. Of the 7 premade spacers 1 failed (14%) due to uncontrolled infection and required hip disarticulation; another one (14%) failed due to fracturing at the stem.

Conclusion: Antibiotic spacers can be readily constructed intra-operatively with off-the shelf components. These offer good outcomes with a low incidence of failure. This may represent a viable treatment option when other types of articulating cement spacers are unavailable.

Gavriel Feuer

Advisor(s): Michael Mont

Biomechanical Comparison of Percutaneous Drilling and Core Decompression for Avascular Necrosis of the Hip: Mechanical Properties

Purpose: Core decompression is a viable treatment option in early stage osteonecrosis of the femoral head. Two separate techniques have been described: standard core decompression with a 9 mm reamer and percutaneous drilling with a 3.2 mm drill. Proximal femoral fracture has been a reported complication of core decompression. We compared these two techniques to determine how drill size affects the biomechanical properties of bone.

Methods: Twenty-four cadaveric femur samples were collected (6 males, 6 females).

Each paired sample was randomly assigned to undergo either percutaneous drilling with multiple passes into the femoral head using a 3.2 mm drill or standard core decompression with a 9 mm entry reamer diameter. Each paired sample was subsequently loaded in a servo-hydraulic materials testing machine to simulate tensile stress on the lateral aspect of the femur. The femur was held in a neutral position and load applied cephalad to the femoral head to generate a varus moment at the lateral aspect. All samples were loaded to failure (fracture). Outcome variables that were measured include the peak force (Newtons, N), deformation (millimeter, mm), femur stiffness (N/mm), and energy (Joules, J).

Results: Percutaneous drilling group had greater amounts of deformation before fracture (16.7 vs 13.1, $p=0.02$), were stiffer (630 vs 615, $p=0.79$), and required more force and energy to fracture (35.7 vs 31.6, $p=0.2$).

Conclusion: Drilling using a 3.2 mm drill resulted in significantly greater potential deformation (varus bending) in the femur prior to fracture (21.6% more potential deformation until failure occurs). The percutaneous drilling group also had greater stiffness and required more energy to fracture, although these were not observed to be significant.

Adam Adler

Advisor(s): Carl Paulino

In-Hospital Mortality Following Open and Closed Long Bone Fracture: A Comparative Study

Background: Open fracture is a serious orthopaedic injury that can lead to significant patient morbidity and mortality. There is limited data on the mortality risk for open compared to closed long bone fracture.

Methods: The Nationwide Inpatient Sample was used to identify all patients who were admitted with a long bone fracture in the United States between 1998 and 2010. Cox proportional hazards regression modeling was used to calculate the hazard ratio (HR) and 95% confidence interval (CI) of mortality.

Results: After adjusting for age, gender, race, insurance, and comorbidities, the HR of mortality was 2.89 (95% CI, 2.56-3.28; $p<0.001$) for open compared to closed fracture. Stratified by anatomical site, the HR of mortality for open compared to fracture was 3.43 for femur (95% CI, 2.78-4.23; $p<0.001$), 2.81 for tibia or fibula (95% CI, 2.17-3.64; $p<0.001$), 2.54 for humerus (95% CI, 1.81-3.56; $p<0.001$), and 1.56 for radius or ulna (95% CI, 1.10-2.23; $p=0.014$).

Conclusions: This data suggests that open fracture carries a worse prognosis compared to closed fracture at the same anatomical site.

Nathan Cornish

Advisor(s): Carl Paulino
Evan Grossman

Increasing Curve Severity is Associated with Worsening Thoraco-Pelvic Coordination in Patients with Adolescent Idiopathic Scoliosis

Purpose: Patients with Adolescent Idiopathic Scoliosis (AIS) have an abnormal ‘in-phase’ gait pattern in the axial plane. This results from dis-coordination of normal pelvic and thoracic rotational relationships during walking. The purpose of this study was to assess the relationship between traditional radiographic measures for AIS and axial plane motion.

Methods: Seventy-two AIS patients, mean 13.7 years and mean Cobb angle 58.1°, were prospectively enrolled for this study. Gait analysis was performed in a 6-DOF motion analysis laboratory at a sampling frequency of 100 Hz. Thirty-four reflective markers were placed on each patient who then performed straight-line walking trials. Patients were stratified based on coronal Cobb angles (10° intervals), central sacral vertical line (CSVL) (10 mm interval), and curve location (right/left, thoracic/thoracolumbar curves). Statistical analysis was performed with a Bonferroni corrected $p < 0.05$.

Results: AIS patients with $< 50^\circ$ curves demonstrated pelvo-thoracic counter rotation during gait. Mean maximal pelvo-thoracic counter rotation was significantly less in AIS (50° curves, an abnormal gait pattern was observed and no pelvo-thoracic counter rotation occurred throughout the gait cycle with a mean maximal pelvo-thoracic counter rotation of 0 degrees, $p = 0.006$). No association between axial plane motion and the other radiographic parameters (CSVL or curve type) were found.

Conclusion: It is well known that severe AIS increases morbidity from cardiopulmonary complications. Our findings demonstrate an association between increasing curve severity and loss of normal physiologic motion in the axial plane. Increasing AIS severity results in stiffness in axial plane motion and a more abnormal ‘in-phase’ gait pattern. These findings suggest that early diagnosis and appropriate treatment before large curves are observed may prevent loss of physiologic motion and prevent a worsening gait pattern in the axial plane.

Dante Leven

Advisor(s): Carl Paulino

Moving Beyond Radiographs: Understanding the Functional Implications of Adolescent Idiopathic Scoliosis Correction in the Coronal Plane

Purpose: Coronal plane malalignment in Adolescent Idiopathic Scoliosis (AIS) patients is the distinguishing feature of severity. With modern treatment techniques resulting in large radiographic coronal curve reductions, understanding the functional implications is the next step. The purpose of this study was to investigate how intraoperative correction techniques alter coronal plane gait parameters.

Methods: Thirty consecutive AIS patients were prospectively enrolled into this study. Analysis was performed in a 6-DOF motion analysis laboratory at a sampling frequency of 100 Hz. Thirty-four reflective markers were placed on each patient who then performed straight-line walking trials pre-operatively and at 1 and 2 yr follow-up. Comparisons of coronal motion were made between the study groups and controls based on the position of C7, the pelvis, and the center of mass. Radiographic parameters including maximal Cobb angle and center sacral vertical line (CVSL) was also calculated. Calculations were performed with custom algorithms. Statistical analysis was performed with Bonferroni-corrected $p < 0.05$.

Results: During gait analysis, control subjects demonstrated 3mm of left-right sway in the coronal plane. Pre-operatively, AIS patients demonstrated 5mm of left-right sway, post-operatively this reduced to 3mm. There was a significant difference in the C7-Pelvis offset in pre-op AIS patients compared to both post-op AIS patients and controls. There was no significant difference between C7-pelvis offset when comparing post-op AIS patients to control patients. However, assessment of gait patterns demonstrated weak correlation ($r^2 = 0.256$, $p = 0.01$) between post-AIS patients and controls.

Conclusion: Our investigation demonstrates that radiographic correction of Cobb angle and CVSL in AIS subjects, results in post-op gait motion similar to controls. It seems the balance center is restored and that left-right sway motion is reduced which in turn decreases energy consumption.

Adam Margalit

Advisor(s): Carl Paulino

Adolescent Idiopathic Scoliosis Curves Cause Restricted Motion and Dis-Coordination of Axial Plane Motion

Purpose: Adolescent Idiopathic Scoliosis (AIS) results in 3-dimensional changes of the spinal curves. However, it is not well understood how these changes affect function. The purpose of this investigation was to evaluate functional differences between control subjects and patients with severe AIS, specifically in the axial plane.

Methods: Seventy-two AIS patients, mean 14.5 years (4M, 11F), with a mean Cobb angle of 57° were prospectively enrolled. Analysis was performed in a 6-DOF motion analysis laboratory at a sampling frequency of 100 Hz. Thirty-four reflective markers were placed on each patient who then performed straight-line walking trials. Pelvic and thoracic motions in the axial plane were compared between the AIS group and controls. Calculation for axial motion, patterns of gait and phase were performed with custom algorithms. Statistical analysis was performed with a Bonferroni-corrected $p < 0.05$.

Results: Control subjects demonstrated a normal ‘anti-phase’ gait pattern. The pelvis and thorax rotate in opposite directions (anti-phase) during the gait cycle, reaching maximum pelvo-thoracic offset at heel strike and then rotating to the opposite direction. The pelvis and thorax cross each other twice during the gait cycle (‘0’ point); once during right single limb stance (24% of gait cycle) and once during left single limb stance (78% of gait cycle). Control subjects had a total pelvic rotation of 9.3° and a combined pelvic-thoracic rotation of 199°. AIS patients demonstrated a mean 44% reduction in total pelvic rotation (5.2°) compared to controls ($p < 0.001$). AIS patients also demonstrated a mean 27% reduction in combined pelvic and thoracic rotation (145°) compared to controls ($p < 0.05$). In AIS patients the pelvis and thorax did not cross at any point, resulting in an abnormal ‘in-phase’ gait pattern.

Conclusion: Our investigation demonstrates that severe AIS results in a restricted gait pattern in the axial plane with reduction in pelvo-thoracic motion.

Jason Oh

Advisor(s): Carl Paulino

Is the Lateral Transpsoas Approach to the Lumbar Spine Safe in Patients with Spinal Deformity?

Introduction: Indications for transpsoas approach to lumbar spine have expanded to include patients with spinal deformities. Approaching the deformity from the curve concavity lets the surgeon modify the concave intervertebral height and correct the coronal curvature. However, anatomical changes may occur in spinal deformity patients. We investigated modifications in lumbar spine anatomy (psoas position (PP), lumbar plexus position (LPP), and vascular structure position (VSP)) in spinal deformity with vertebral rotation (VR).

Methods: Lumbosacral MRIs (L1-S1) from right-convex thoracic (left-convex lumbar) adolescent idiopathic scoliosis (AIS) patients were analyzed. The anterior vertebral body (AVB) axis was used as reference line. Parameters evaluated at each level included VR, PP, psoas diameter (PD), LPP, and VS. Paired t-test analyses were used to describe differences between concave and convex aspect of the curve.

Results: 50 AIS patients (17M, 33F) with a mean 49.8° (13°-91°) thoracic Cobb and a mean 42.3° (8°-75°) lumbar Cobb were analyzed. Mean VR at each level were L5-S1=2.6°, L4-5=4.8°, L3-4=6.5°, L2-3=7.7°, L1-2=6.9°. We found significant differences ($p < 0.05$) between concave-convex (right-left) LPP at each level (L5-S1=2.2mm, L4-5=2.2mm, L3-4=4.2mm, L2-3=5.1mm, L1-2=3.7mm). A significant correlation was found between increasing VR and concave-convex LPP difference ($r = 0.68$, $p < 0.001$). These changes were corrected for with a true lateral projection of the intervertebral space. VSP were also within the surgical corridor. These structures were more at risk on the curve concavity.

Conclusion: Care must be taken during the transpsoas approach to the lumbar spine in patients with rotational deformities. This study demonstrates a significant anterior shift in the concave lumbar plexus with VR towards curve convexity. Careful preoperative planning, patient positioning, and meticulous dissection are paramount for the prevention of lumbar plexus/vascular injury.

Ashish Patel

Advisor(s): Carl Paulino

Moving Beyond Radiographs; Functional Changes in the Sagittal Plane after Adolescent Idiopathic Scoliosis Realignment and Fusion

Purpose: The sagittal plane is the primary factor in successful clinical outcomes in patients with adult spinal deformities. Restoring sagittal plane alignment and function is critically important during all spinal procedures. The purpose of this study was to determine the dynamic properties in the sagittal plane after posterior spinal fusion for Adolescent Idiopathic Scoliosis (AIS).

Methods: Thirty consecutive AIS patients were prospectively enrolled into this gait analysis study. Analysis was performed in a 6-DOF motion analysis laboratory at a sampling frequency of 100 Hz. Thirty-four reflective markers were placed on each patient who then performed straight-line walking trials pre-operatively and at 1 and 2 yr follow-up. Sagittal marker data including C7-Pelvis offset and C7-Pelvis motion were calculated to determine the pre-post sagittal motion. Statistical analysis was performed with a Bonferroni-corrected $p < 0.05$ for significance.

Results: In control subjects, the C7 marker was a mean 51.9mm posterior to the center of the pelvis (C7-Pelvis offset). C7-Pelvic motion was found to be 20mm (range 43-63) during a gait cycle. AIS patients ambulated significantly anterior to control subjects (C7-Pelvic offset=35mm) with a significantly less C7-Pelvic motion of 15mm (range 28-43). Postoperatively, the C7-Pelvis shifted posteriorly to 49.7mm ($p < 0.01$) and sagittal plane motion was found to increase 25% to 20mm (range 40-60). In fact, cross-correlation of the post-operative sagittal C7-Pelvic offset during a gait cycle demonstrated a pattern that mirrored the control group ($R = 0.98$; $p < 0.001$).

Conclusion: Posterior spinal fusion and realignment in AIS patients resulted in sagittal plane posture and C7-Pelvic offsets that significantly mirrored control subjects during straight line walking. Although favorable realignment may be obtained, long-term studies are required to investigate the evolution of sagittal plane motion and function post-AIS fusion and the unfused segments.

Paul Perdue

Advisor(s): Carl Paulino

Risk Factors for Hardware Removal Following Fracture of the Tibia or Fibula: A Nationwide Database Study

Purpose: Indications for open reduction and internal fixation (ORIF) of tibia and/or fibula fractures vary, however, some patients require removal of hardware (ROH) for various complications. Currently, there are limited data evaluating the epidemiology of and risk factors for ROH of the tibia/fibula. We examined the associations between tibia/fibula fractures and: (1) characteristics of fractures requiring ORIF; (2) indications for ROH; (3) demographic risk factors for ROH; (4) length of stay; and (5) total hospital charges.

Methods: The Nationwide Inpatient Sample (NIS) was used to identify patients admitted for tibia/fibula ORIF and ROH between 1998-2010 in the United States. We used ICD-9 diagnosis codes to identify fracture locations, comorbidities, and indications for ROH. We identified 1,610,149 ORIF patients, and 56,864 patients (3.5%) who underwent ROH. Logistic regression analyses and independent sample t-tests were used to assess risk factors and differences.

Results: Among fractures requiring ORIF, the most common was for both tibia/fibula. The most common indications for ROH were implant infection and osteomyelitis. Risk factors for ROH included men and Deyo comorbidity scores of 1 and 2 or greater. Asians or Pacific Islanders were significantly less likely to undergo ROH. The length of stay and total charges were significantly higher for ROH patients than ORIF only.

Conclusions: Hardware removal is a serious complication following ORIF for fractures of the tibia/fibula. The results of the current study suggest that gender, presence of co-morbidities, and payer status were all significant factors in predicting hardware removal for the tibia/fibula following ORIF.

Robert Pivec

Advisor(s): Carl Paulino

De-Rotational Maneuvers during Surgical Realignment for Adolescent Idiopathic Scoliosis. Are we Doing Enough?

Purpose: Intraoperative de-rotational maneuvers using pedicle screw fixation attempts to restore axial plane alignment. Previous studies have found severe AIS subjects to have an abnormal ‘in-phase’ gait in the axial plane compared to control subjects. The objective of this study was to evaluate axial plane motion in AIS patients’ pre- and postoperatively and compare these findings with asymptomatic controls.

Methods: Thirty consecutive AIS patients were prospectively enrolled into this gait analysis study. Analysis was performed in a 6-DOF motion analysis laboratory at a sampling frequency of 100 Hz. Thirty-four reflective markers were placed on each patient who then performed straight-line walking trials pre-operatively and at 1 and 2 yr follow-up. Comparisons of axial plane pelvic and thoracic motion were made between pre, post and control groups. Statistical analysis was performed with a Bonferroni corrected p value < 0.05 for significance.

Results: As previously reported, pre-op AIS patients demonstrated an abnormal ‘in-phase’ pelvic and thoracic rotation. Pre-op patients had restricted motion to the right and no counter rotation throughout the gait cycle. Control subjects demonstrated a normal ‘anti phase’ rotation with counter-rotation at 24% and 78% of the gait cycle. Post-operative AIS patients had notable improvements in pelvic and thoracic rotation with counter-rotation occurring at 38% and 65% of the gait cycle and an increase in maximal thoracic rotation to the right from 0.01 (pre-op) to 1.60° (post-op; p=0.034).

Conclusion: AIS patients have restricted motion in the axial plane and demonstrate an abnormal ‘in-phase’ gait pattern. Although improvements were noted in post-operative patients, no patient demonstrated axial plane gait parameters similar to normal controls. Greater emphasis could be made to axial plane correction during AIS re-alignment procedures.

Yoseph Rosenbaum

Advisor(s): Carl Paulino

Risk Factors for Removal of Hardware Following Fracture of the Radius and/or Ulna: A Nationwide Database Study

Purpose: Open reduction and internal fixation (ORIF) has been shown to be an effective treatment for fractures of the radius and/or ulna, but complications can occur, including persistent pain, malunion, nonunion, and infection, which may necessitate removal of hardware (ROH). Currently, there is a paucity of literature describing the epidemiology of and risk factors for ROH of the radius and/or ulna.

Methods: Using the Nationwide Inpatient Sample, we identified 423,727 patients who were admitted for ORIF of the radius and/or ulna between 1998 and 2010, and identified 12,868 patients (3.0% of ORIF admissions) who underwent ROH. We used ICD-9 diagnosis codes to identify patient comorbidities and indications for ROH.

Results: Over the study period, the most common indications for ROH were implant infection (38%) and mechanical complications (22%). Risk factors for ROH included male gender (OR=1.36; p<0.001), white race (OR=1.25; p=0.016), and a Deyo comorbidity score of 1 (OR=1.49; p<0.001), 2 (OR=1.58; p<0.001), or ≥3 (OR=1.79; p<0.001). Length of stay was 3.20 (95% CI=3.17-3.23) days and hospital charges were \$26,870 (95% CI=26,615-27,125) for ORIF, and ROH accounted for an additional 4.33 (95% CI=4.09-4.57) days in the hospital and \$24,073 (95% CI=22,879-25,266) in charges.

Conclusion: Removal of hardware following ORIF for radial and/or ulnar fractures is an infrequent but serious complication that increases patient morbidity and causes a burden to both patients and providers. Patient demographics of male gender, white race, and multiple comorbid conditions were identified as independent risk factors for ROH. Further studies are needed to evaluate the association of specific comorbidities with ROH.

Martin Pendola

Advisor(s): Subrata Saha

Microwave Sintering of Glass Ceramics

Ceramics show mechanical properties, esthetics and biocompatibility highly desired for dentistry. However, these ceramics require a prolonged sintering process to produce the material, including a slow controlled cooling process to avoid cracks. This process may take up to 16 hours in a conventional furnace, with a large energy consumption.

Microwave sintering has been used to heat materials in industry. When compared with conventional sintering, the heating times are shorter and the energy consumption is reduced.

Previous research in our lab shows dental ceramics can be sintered with Microwave Hybrid Sintering, in a shorter process that may improve the mechanical properties of the material.

Hypothesis: MHS can be used to sinter the new generation of dental glass-ceramics. We also plan to investigate if an improvement in the mechanical properties of the dental ceramics can be achieved with MHS. Materials and Methods: Samples of lithium disilicate glass ceramics will be sintered using MHS and conventional sintering. The produced samples will be tested (density, hardness, flexural strength) and analyzed (X-rays diffraction) to compare the mechanical properties and microstructure of the material. Results: MHS process produced the ceramic materials in shorter times when compared to conventional sintering. The mechanical properties of lithium disilicate glass ceramics appear to be improved using MHS. Hardness is increased in samples sintered using MHS (652 HV + 23) when compared with conventional sintering (567 HV + 14) and flexural strength is also improved for MHS process (454 MPa + 51 vs 304 MPa + 75). X-Ray Diffraction shows an increase of the crystalline phase in samples sintered with MHS, which may explain the improvement of the mechanical properties.

Conclusion: MHS is an alternative for sintering dental ceramics, including the most recent dental glass ceramics, and improving the mechanical properties of the material.

Rozan Wynter

Advisor(s): Subrata Saha

Relationship Between Material and Mechanical Properties of Osteophytes and Non-osteophytic Cortical Bone: A Preliminary Study

Several studies have associated the development of spinal osteophytes with disc degeneration. Others have characterized them as adaptive bone remodeling in response to unusual stress/strain conditions. No recent study examined the microstructure and mechanical properties of osteophytes.

Lumbar vertebrae and femurs were harvested from eight different cadavers (average age: 75 years old). Vertical beams (18-24mm X 3-5mm X 2-3mm) and cubes (3mm³) were taken from the vertebral anterolateral cortex (non-osteophytic), vertebral osteophytes, and from the femoral diaphysis. Radiological density was obtained with a Faxitron X-rayTM machine. Microhardness tests were performed on resin-embedded cubes using a Vickers diamond micro-indenter, whereas the beams were tested for three-point bending. Each specimen was then divided into two parts. One side was used for undecalcified histology while the other was used for material and ash density measurements.

Vertebral osteophytes had an average of 27.99 HV (hardness value), while the sample of femoral cortical bone had a HV of 45.94. The maximum load to failure (at 3 point bending) for osteophytic and non-osteophytic vertebral cortex specimens was 64 and 4 Newtons (N), respectively. Material density (D_{mat}) for cortical bone ranged from 1.4 to 2.0 g/cm³, whereas D_{mat} for the osteophytes was between 1.18 and 1.70 g/cm³. Additionally, there was no correlation between the relative hardness of the osteophytes and the material density but there was a positive correlation with the radiological (areal or optical) density and ash density. Histological analysis showed disorganized osteons with small haversian canals for the osteophytes as compared with normal osteons from non-osteophytic specimens.

Vertebral osteophytes have higher load carrying capacity than vertebral cortical bone. However, cortical bone (vertebral and diaphyseal) presents a more mature and organized microstructure than osteophytes.

Fred Xavier

Advisor(s): Subrata Saha
Kay Beharry, Gloria Valencia

Regional Variations In Microstructure And Biomechanical Properties Of The Human Vertebral Endplate And Trabecular Bone

Spinal osteoporosis affects predominantly the anterior part of the vertebrae leading to its collapse and kyphosis. However, limited data are available on the biomechanical properties of different regions within the vertebral endplate and cancellous bone. Does bone resorption occur at a higher rate in the anterior than in the lateral region of the vertebra?

Thoracic (T10) and lumbar (L4-L5) vertebrae were harvested from fifteen human cadaveric spines (average age: 77 years old). Twelve cylindrical cores of 7.24 mm (diameter) by 3.15 mm (height) were prepared from each vertebral body. Shear strength was measured using a stainless steel tubular blade. Optical and bulk densities were calculated before mechanical testing. Apparent, material, and ash densities were measured after testing. Undecalcified histology was performed for histomorphometric analysis.

Mechanical strength increased by an average of 30% from central to lateral regions of both endplate and cancellous bone. As calculated by one-way ANOVA, shear strength changed within the three main (anterior, central, lateral) endplate regions. A Tukey post-hoc test revealed that the shear strength was significantly lower ($p = 0.04$) in the anterior (0.44 ± 0.06 MPa) compared to the lateral region (3.09 ± 0.71). There was also an average decrease in endplate maximum load of 29% from the inferior to the superior regions. Mechanical strength positively correlated with material and ash densities. Histological analysis showed a decrease in the ratio osteoid/bone surface (OS/BS) by 20% from superior to inferior bony endplates.

Results from this study may explain the relationship between vertebral fracture patterns and osteoporosis. Consequently, newer implants for spinal interbody fusion could optimize the loading in the lateral aspects of the endplate and reduce the likelihood of subsidence.

Robert Borzio

Advisor(s): William Urban

Predictors of Septic Arthritis in the Adult Population

Purpose: Septic arthritis is a devastating condition that requires a timely diagnosis to minimize articular damage and the associated high rate of morbidity and mortality. Our objective was to analyze patient factors and laboratory parameters, which may be associated with a diagnosis of septic arthritis.

Methods: Serum and synovial leukocyte counts and differentials were compared between a group of patients who had culture-positive septic arthritis ($n=22$) and those who had negative cultures ($n=436$).

Results: Within the combined cohort, 22 had septic arthritis (SA) confirmed by a positive synovial fluid culture. Of these, 15 patients (68%) had a positive gram stain with the majority identified as *Staphylococcus Aureus*. The non SA group was older than the SA group (61.6 vs. 51.2, $p=0.012$). History of fever, temperature, number of comorbidities, weight bearing status, ESR, serum WBC, and serum neutrophil percentage were non significant ($p>0.05$). Platelet count was higher and hematocrit was higher in the SA group ($p=0.017$ and $p=0.018$ respectively).

Synovial fluid white blood cell count was 26,758 for the non SA group and 70,581 for the SA group ($p=0.001$).

Conclusion: This study calls into question the usefulness of serum laboratory values that are typically ordered in the work-up of an acutely swollen joint, none of which were significantly different when comparing the SA and non SA groups. This suggests that the diagnosis relies heavily on clinical examination and synovial fluid analysis. A synovial fluid WBC of greater than 64,000 yielded the optimal combination of sensitivity and specificity, and the PMN percentage was not significant in comparing the cohorts.

Matthew Boylan

Advisor(s): William Urban

Venous Thromboembolism Following Hip and Knee Arthroplasty: Is There A Difference in Risk For Primary Compared to Revision Surgery?

Purpose: Venous thromboembolic events (VTE) remain a feared complication following total hip (THA) and total knee (TKA) arthroplasty. Although incidence and risk factors of VTE following primary THA and TKA have been well described, reports on revision THA and TKA are rare. The purpose of this study was to compare the incidence of VTE within 90 days postop for primary versus revision THA and TKA.

Methods: The NY Department of Health Statewide Planning and Research Cooperative System (SPARCS) was used to identify primary and revision THA and TKA cases between 2003 and 2012. We used an encrypted patient identifier to track patients for 90 days postop. Patients admitted with VTE were identified using ICD-9 codes for deep venous thrombosis (DVT) and pulmonary embolism (PE). Patients who had a history of PE at the time of surgery were excluded. Logistic regression was used to calculate the odds ratio (OR) and 95% confidence interval (95% CI) of VTE within 90 days for primary versus revision THA and TKA.

Results: THA or TKA was performed in 343,387 patients, among which 331,672 were primary and 11,715 were revision cases. Incidence of VTE within 90 days was 1.75% for primary (N=5,794) and 1.45% (N=170) for revision cases. After controlling for age, sex, race, and comorbidities, revisions were at 22% decreased risk of VTE (OR=0.78; 95% CI=0.66-0.92; p=0.003). Upon stratification by anatomical location, risk of VTE was decreased for revision compared to primary TKA (OR=0.69; 95% CI=0.55-0.88; p=0.002), and had no difference for revision compared to primary THA (OR=0.96; 95% CI=0.76-1.20; p=0.693).

Conclusion: We found that the risk of VTE was similar for primary and revision THA and TKA. Revision arthroplasty may involve greater intraoperative joint injury, longer operative time, and longer recovery time compared to primary arthroplasty, however, our data suggest that these potential exposures do not affect overall risk of postop VTE.

Dipal Chatterjee

Advisor(s): William Urban

Acromioclavicular Joint Reconstruction Using a Tendon Graft: Comparing a Standard Tendon Graft to a Novel 'Sutured Through-out' Tendon Graft

Purpose: With a recurrence rate of over 30%, techniques that offer stronger acromioclavicular (AC) joint reconstruction through increased graft strength may provide longevity. The purpose of our study was to determine the biomechanical strength of a tendon graft sutured throughout compared to a native tendon graft in

Grade 3+ anatomical AC joint reconstruction.

Methods: For this in vitro experiment 9 paired (n=18) cadaveric AC joints of 3 males and 6 females (age 86 years, range 51-94) were harvested. Anatomic repair with fresh bovine Achilles tendon grafts without bone block was simulated. Specimens were divided into two groups; with group 1 using grafts with UHMWPE suture ran throughout the whole length. In group 2, reconstruction with only native allografts was performed. The distal scapula and humerus were casted in epoxy compound and mounted on the mechanical testing machine. Tensile tests were performed using a mechanical testing machine at the rate of 50 mm/min. Maximum load and displacement to failure were collected.

Results: The average load to failure was significantly higher for group 1 compared to group 2, with mean values of $437.5 \text{ N} \pm 160.7 \text{ N}$ and $94.4 \text{ N} \pm 43.6 \text{ N}$, (p = 0.001). The average displacement to failure was not significantly different, with $29.7 \text{ mm} \pm 10.6 \text{ mm}$ in group 1 and $25 \text{ mm} \pm 9.1 \text{ mm}$ in group 2, (p = 0.25).

Conclusion: We conclude that a UHMWPE suture reinforced graft can provide a 3.6 times stronger AC joint reconstruction compared to a native graft.

Dean Perfetti

Advisor(s): William Urban

Biceps Tenodesis and Hospital Admission Following SLAP Repair: What Are the Risk Factors?

Purpose: Superior labrum anterior and posterior (SLAP) tear presents with shoulder pain and decreased joint function. There is a paucity of data on risk factors for postoperative complications and surgery failures. We investigated the associations between patient- and surgery-level risk factors and the risk of shoulder reoperation with biceps tenodesis or hospital admission following primary SLAP repair.

Methods: The NY Department of Health Statewide Planning and Research Cooperative System (SPARCS) was used to identify patients who underwent SLAP repair between 2003 and 2011. Patients were tracked for 1 year postop. We calculated odds ratio (OR) and 95% confidence interval (95% CI) of biceps tenodesis within 1 year and hospital admission within 90 days, according to the patient factors of age, gender, race, and comorbidities, and the surgical factors of operating time, surgeon volume, and facility volume.

Results: We identified 31,398 primary SLAP repair patients. Biceps tenodesis within 1 year was observed in 6.8%, while hospital admission within 90 days was observed in 1.4% of patients. Risk factors for biceps tenodesis included white race (OR=1.29; $p<0.001$) and female sex (OR=1.16; $p=0.005$). Operation time < 1 hour was associated with decreased risk of biceps tenodesis (OR=0.87; $p=0.028$). Risk factors for hospital admission included age > 45 years (OR=1.51; $p<0.001$), white race (OR=1.29; $p=0.046$), and one or more comorbidities (OR=2.48; $p<0.001$). High facility volume (>6 SLAP repairs/month) was associated with decreased risk of admission (OR=0.68; $p=0.030$).

Conclusion: The findings of this study can help orthopaedic surgeons to preoperatively identify patients at higher risk of postoperative complications following primary SLAP repair. Further investigation of the protective effects of decreased operating time and high facility volume may reveal potential areas for improvement of patient care.

David Frumberg

Advisor(s): Jaime Uribe

Rotational Deformity of the First Ray Precludes Accurate Distal Metatarsal Articular Angle Measurement in Hallux Valgus

Purpose: The distal metatarsal articular angle (DMAA) is used to assess correction of hallux valgus postoperatively. Measurement of the DMAA in one plane may not accurately assess the rotational component of this 3-dimensional deformity. No studies have examined this angle in situ for accuracy.

Methods: The diaphysis of the 1st metatarsus and the 1st metatarsophalangeal joint of 8 cadavers were dissected and fixed with a cylindrical bolt passed transversely through the talus. The bolt was placed both perpendicular to the long axis of the metatarsus and parallel to the plane of simulated weight-bearing of the foot. Initial AP X-rays were taken at 15° caudad. The foot was then dorsiflexed 90° and a longitudinal X-ray was obtained to verify the initial rotation. A transverse, diaphyseal osteotomy of the first metatarsal was performed. The distal fragment was internally rotated 15° and an AP image was obtained. The specimen was dorsiflexed 90° and a longitudinal X-ray was obtained for measurement of axial rotation. This was repeated for 30, 45, and 60° of internal rotation of the distal fragment.

Results: Pearson correlation (0.97) was positive between the pre-set and measured angle ($p<0.001$). This confirmed accuracy of the pre-set angles. IMA remained stable for each AP image despite rotation of the distal segment ($\alpha<0.05$). This demonstrated that rotation occurring through the first metatarsal osteotomy contributed no additional angulation to the metatarsal alignment. The DMAA was not constant with rotation through the osteotomy site. It differed significantly from baseline ($\alpha<0.05$) as distal segment rotation increased. There was no significant trend of variance.

Conclusion: Measurement of the DMAA varies significantly with rotation of the distal first metatarsus. Caution is advised using the DMAA to assess first MP joint congruency, as it may unreliably and inaccurately estimate the 3-D deformity often encountered in pathologic hallux valgus.

Rachael Jennings-Charles

Advisor(s): Mohamed Boutjdir

Expression and Regulation of calcium channels in Human Heart Failure

Heart failure (HF) is a major and growing public health problem, affecting more than 20 million people worldwide. Despite the progress in HF management over the years, its pathophysiology is still not well understood. We and others have previously shown that some fetal genes normally not expressed in the adult ventricle are re-expressed in the failing heart. Given that weak myocardial contractility is often associated with HF, we hypothesized that the fetal gene, Cav1.3 L-type Ca channel (CACVA1D), is re-expressed in Human HF to provide additional Ca entry into the cell and thus better contractility.

Using qRT-PCR analysis on failing Human heart tissue, the data showed increased CACNA1D and CACNA1C (another L-Type Ca channel, Cav1.2) mRNA levels relative to normal tissue. Furthermore, imaging and lenti-virus infection of cultured neonate rat ventricular myocytes (NRVMs) and mouse atrial cell lines (HL-1) demonstrated that the C-terminal of the CACNA1D protein, Cav1.3, is cleaved from the main $\alpha 1$ subunit protein and translocates to the nucleus where it acts as a transcription factor. A fragment of the C-terminus of Cav1.3 increased transcription of both CACNA1D and CACNA1C in NRVMs but has the opposite effect in HL-1 cells. The site (s) on the promoter region where the C-terminus regulates the gene expression is underway using promoter deletion constructs and luciferase assays.

Altogether, the data are the first to demonstrate the re-expression of a fetal Ca channel gene in Human HF and its up regulation by its own C-terminus leading to improved cardiac contractility. These novel findings are useful for ionotropic therapy in the treatment of HF

Florenal Joseph

Advisor(s): William Chirico

Role of Yeast PARK9 in Plasma Membrane Repair in *Saccharomyces cerevisiae*.

Cell membrane repair is critical for survival of damaged eukaryotic cells. Plasma membrane repair is a complex process that utilizes membrane vesicles derived from lysosomes and perhaps other sources. One of the repair pathways that has been investigated is membrane patching, which involves the influx of extracellular Ca^{2+} to trigger vesicle-vesicle fusion leading to the formation of a membrane patch. The patch fuses with the cell membrane at the damage site. Despite active investigations of the cell membrane repair, the mechanism of repair remains poorly understood.

The long-term goal of the lab is to develop a comprehensive understanding of membrane repair. We are using *Saccharomyces cerevisiae* as model system to identify membrane repair genes and define their role in repair. Our preliminary genomic screen of nearly 5000 yeast strains each harboring a complete deletion of an individual gene revealed about 300 candidate genes involved in membrane repair. We are focusing on a gene, which is a divalent cation transporter that is located in the vacuolar membrane and shares homology with a human gene implicated in Parkinson's disease. I propose to investigate the contribution of this gene to cell membrane repair. Our research may yield insights into the progression and treatment of Parkinson's disease.

Sara Abou Merhi

Advisor(s): M.Mahmood Hussain

MicroRNA-30c (miR-30c) in lipid metabolism and in treating hyperlipidemia and atherosclerosis

Hyperlipidemia is a risk factor for atherosclerosis (athero). A way to reduce hyperlipidemia is to curtail the entry of lipoproteins in circulation. Lipoprotein assembly requires apolipoprotein B (apoB) and microsomal triglycerides transfer protein (MTP). Hyperlipidemia can be reduced with statins, MTP inhibitor, and apoB anti-sense oligonucleotide. But, many patients on these drugs either develop hepatic steatosis or are intolerant. So, there is a need for new drugs that reduce hyperlipidemia and athero without causing side effects. Our lab has shown that lentiviral-mediated hepatic expression of the microRNA-30c (miR-30c), derived from miR-30c-1 and miR-30c-2 genes, reduces plasma lipids and athero in Western diet fed mice without causing steatosis. In contrast, miR-30c inhibition increases plasma cholesterol and athero. Based on these, we hypothesize that endogenous miR-30c regulates plasma and tissue lipids and miR-30c mimic can be used to treat hyperlipidemia and athero.

To test whether endogenous miR-30c regulates lipid metabolism, we deleted miR-30c-1 and miR-30c-2 genes using specific transcription activator-like effector nucleases (TALENs) in mouse and human hepatoma cells. Knockdown of individual genes increased MTP expression and media apoB. Knockdown of both genes had an additive effect on MTP and apoB. We used these TALENS to generate single and double miR-30c-1 and miR-30c-2 gene knockout mice to address how miR-30c regulates lipid metabolism.

To evaluate therapeutic potential, we injected a miR-30c mimic in C57B16 and Apoe^{-/-} mice fed a western diet. miR-30c mimic reduced diet-induced hyperlipidemia in C57B16 and Apoe^{-/-} mice without causing hepatic steatosis. Additionally, miR-30c mimic regressed athero in Apoe^{-/-} mice. These studies provide the evidence that endogenous miR-30c regulates MTP expression and the proof of concept that miR-30c mimic can be used as a beneficial treatment modality to lower plasma lipids and reduce athero.

Liye Zhou

Advisor(s): Mahmood Hussain

Identification of Human MicroRNAs Modulating ApoB And ApoAI Secretion

Cardiovascular diseases (CVD) are the leading cause of death in the US. High plasma LDL and low HDL are the major risk factors of CVD. Therefore, drugs that can lower LDL and increase HDL without adverse effects might be useful in the treatment of CVD. MicroRNAs are small non-coding RNAs that target multiple mRNAs to modulate diverse biological pathways. We hypothesized that miRs exist in nature that could simultaneously lower apoB (LDL scaffolding protein) and increase apoAI (major HDL protein) secretion, which could be beneficial in treating diseases. To test this, I screened a library of 1237 human miRs and identified three miRs that decreased apoB and increased apoAI secretion from human hepatoma cells. MiR-1200 was studied further as it was more potent in differentially regulating apoB and apoAI secretion. Bioinformatics analysis suggested that miR-1200 targets 3'-untranslated regions (3'-UTR) of both apoB and MTP mRNA. Overexpression of miR-1200 reduced apoB and MTP mRNA levels by enhancing posttranscriptional degradation. Mechanistic studies showed that miR-1200 interacts with 3'-UTRs of apoB and MTP. In contrast, miR-1200 increased apoAI protein secretion and mRNA expression without affecting mRNA stability. Therefore, we hypothesized that miR-1200 increases apoAI expression by targeting repressors of apoAI transcription. We selected 5 repressors that were predicted targets of miR-1200 to perform a siRNA screening. Silencing of BCL11B increased apoAI mRNA by 2-fold and secretion by 50% with no effect on apoB. Individual and combined transfections of siBCL11B and miR-1200 had similar effects on apoAI secretion suggesting that miR-1200 might increase apoAI secretion by reducing BCL11B expression. In short, our studies showed that miR-1200 reduces apoB secretion and increases apoAI secretion by two different mechanisms. Future study will focus on the in vivo effects of hepatic overexpression of miR-1200 on lowering plasma lipids and CVD in mice.

Hui Jiang

Advisor(s): Xian-cheng Jiang

Adipocyte phospholipid transfer protein and lipoprotein metabolism.

Objective: Phospholipid transfer protein (PLTP) is highly expressed in adipose tissues. Thus, the effect of adipose tissue PLTP on plasma lipoprotein metabolism was examined.

Approach and results: We crossed PLTP-Flox- Δ Neo and adipocyte protein 2 (aP2)-Cre recombinase (Cre) transgenic mice to create PLTP-Flox- Δ Neo/aP2-Cre mice that have a 90 and a 60% reduction in PLTP mRNA in adipose tissue and macrophages, respectively. PLTP ablation resulted in a significant reduction in plasma PLTP activity (22%), high-density lipoprotein-cholesterol (21%), high-density lipoprotein-phospholipid (20%), and apolipoprotein A-I (33%) levels, but had no effect on nonhigh-density lipoprotein levels in comparison with those of PLTP-Flox- Δ Neo controls. To eliminate possible effects of PLTP ablation by macrophages, we lethally irradiated PLTP-Flox- Δ Neo/aP2-Cre mice and PLTP-Flox- Δ Neo mice, and then transplanted wild-type mouse bone marrow into them to create wild-type \rightarrow PLTP-Flox- Δ Neo/aP2-Cre and wild-type \rightarrow PLTP-Flox- Δ Neo mice. Thus, we constructed a mouse model (wild-type \rightarrow PLTP-Flox- Δ Neo/aP2-Cre) with PLTP deficiency in adipocytes but not in macrophages. These knockout mice also showed significant decreases in plasma PLTP activity (19%) and cholesterol (18%), phospholipid (17%), and apolipoprotein A-I (26%) levels. To further investigate the mechanisms behind the reduction in plasma apolipoprotein A-I and high-density lipoprotein lipids, we measured apolipoprotein A-I-mediated cholesterol efflux in adipose tissue explants and found that endogenous and exogenous PLTP significantly increased cholesterol efflux from the explants.

Conclusions: Adipocyte PLTP plays a small but significant role in plasma PLTP activity and promotes cholesterol efflux from adipose tissues.

Inamul Kabir

Advisor(s): Xian-cheng Jiang

The effect of phosphatidylcholine (PC) remodeling on triglyceride-rich lipoprotein production and metabolism

Triglyceride-rich lipoproteins (TRL) and their metabolism are closely related to dyslipidemia. Phosphatidylcholine (PC) is the major lipid on the surface of all lipoproteins including TRL. An important aspect of phosphatidylcholine (PC) metabolism is that PC synthesized through the de novo pathway on glycerol-3-phosphate backbone undergoes extensive remodeling via the Lands' Cycle and this process influences cellular membrane PC compositions. One key enzyme in the Lands' Cycle is acyl-CoA:lysophosphatidylcholine acyltransferase (LPCAT) which utilizes lysophosphatidylcholine (LysoPC) and acyl-CoA to produce polyunsaturated PC by removing saturated fatty acid at sn-2 position of PC followed by the addition of a polyunsaturated fatty acid, especially linoleic acid and arachidonic acid, at the same position. There are four isoforms of this enzyme. LPCAT3 is the major isoform in small intestine and liver where TRLs are produced. Therefore, it is conceivable that proper LPCAT3 activity is critical for both hepatocyte and enterocyte TRL production and metabolism. In this study, we utilized liver and intestine-specific Lpcat 3 deficient mice using Ad-Cre and inducible Cre-LoxP system respectively to test our general hypothesis that LPCAT3 activity is crucial for TRL production and plasma TRL levels. Our preliminary data suggest that genetic ablation of Lpcat3 in small intestine and liver separately decreased plasma triglyceride levels which can be rescued by the infusion of linolenyl phosphatidylcholine (18:1) and arachidonyl phosphatidylcholine (20:4) in vivo. There was a gross morphological change in the villi structure in LPCAT3 deficient small intestine. Importantly, it is well known that Lpcat 3 is located downstream of liver X receptor (LXR) and PPAR γ , thus the effect of LXR or PPAR γ on TRL could be mediated by LPCAT3, at least partially.

Mukta Asnani

Advisor(s): Tatyana Pestova
Christopher Hellen

Mechanism of Initiation on the Cadicivirus-A IRES

Cadicivirus-A (CDV-A), a recently discovered picornavirus, is unique in this family in having a dicistronic genome, with putative IRESs in the 5'UTR and intercistronic region. The relatedness between CDV-A and Poliovirus (PV) IRESs and between coding regions of CDV-A and Rosaviruses suggests that CDV-A likely acquired its IRESs as a result of multiple recombination events during replication. We undertook a study of these IRESs to identify potentially novel mechanisms of IRES-mediated initiation and to gain insights into IRES evolution. IRES is cis-acting highly structured RNA element composed of multiple modules or domains which come together and help ribosome to land internally onto RNA. A model of the CDV-A 5'UTR was derived by bioinformatic analysis and chemical probing. It consisted of 14 domains (A-N). In vitro translation and reconstitution showed that the functional activity of the CDV-A IRES requires domains K-M, and is substantially enhanced by domains H-J. In vitro reconstitution experiments also revealed that like in the case of the PV IRES, 48S complex formation on the CDV-A IRES required eIF2, eIF3, eIF4A, eIF4G and the IRES trans-acting factor PCBP2, but in contrast to the PV IRES, was also dependent on eIFs 1 and 1A. 48S complex formation was also enhanced by eIF4B. PCBP2's three KH domains bound to the four-way junction of domain K and to apical sites in it close to the tetraloop, whereas eIF4G bound specifically to domain M, and recruited eIF4A to its vicinity. These interactions are comparable to interactions of these factors with the PV IRES, but unlike it, the CDV-A IRES did not depend on an interaction between eIF4G and eIF3 for ribosomal recruitment. This observation indicates that eIF4G must have functions other than simply as a point of attachment for eIF3, and that recruitment of 43S complexes to the IRES must depend on interactions of the IRES with other factors and/or with the 40S subunit itself.

Kamala Anumukonda

Advisor(s): Christopher Roman

The role of TFEB/TFE3 in Macrophage Development and Function

Autophagy is important for macrophage development and their immunological functions. First, monocytes must up-regulate autophagy in order to differentiate into macrophages. Once mature, macrophages also need autophagy for efficient phagocytosis of intracellular bacteria, antigen presentation via MHC II to CD4 T cells, host antiviral defense, antifungal responses and activation of defense against gram-negative bacteria via TLR signaling.

Recently, a transcription factor we study in the lab, TFEB, has been implicated by others in the regulation of genes involved in autophagy and lysosomal biogenesis. TFEB and its close relative TFE3 belong to the MiT family of transcription factors. They share sequence homology and DNA binding properties.

Given the importance of autophagy to macrophage function, I have been studying the role of TFEB in autophagy in macrophages. One in vitro approach is using transformed RAW 264.7 macrophages in which autophagy and lysosome biogenesis can be activated. A second one is using primary bone marrow (BM) derived macrophages in vitro from mice conditionally deficient in TFEB alone or both TFEB and TFE3 (dko). Using these mice, I studied macrophage differentiation by inducing sterile peritonitis.

My preliminary studies show that in RAW cells, TFEB abundance and nuclear localization is responsive to multiple immunological stimuli that activate autophagy such as pathogen associated molecules like LPS from E.coli, cytokines like IFN- γ involved in antiviral defense, and the mTOR inhibitor Rapamycin. In contrast, using BM cells from conditional TFEB null mice and dko mice, I show that TFEB and TFE3 are dispensable for differentiation of monocytes into macrophages both in vitro and in vivo. I would like to investigate if TFEB/TFE3 mediated autophagy is important in antimicrobial defense.

Nanda Lahiri

Advisor(s): Christopher Roman

Role of TFE3 and TFEB in T cells

The MiT family of transcription factors consists of four members, TFE3, TFEB, MiTF and TFEC. TFE3 and TFEB have been shown to be involved in T-cell dependent antibody responses in activated CD4⁺ T cells and thymus dependent humoral immunity. TFEB together with TFE3 can induce CD40L expression (a surface antigen on activated T cells), which interacts with CD40 on the surface of B cells and promotes antibody production. It has been shown that by inactivating TFE3 and TFEB, in mice expressing the trans dominant negative (TDN) protein, in T cells only, the expression of CD40L is impaired when compared to WT mice. However we are yet to determine a clearer picture of the regulation of CD40L by TFE3 and TFEB. To this effect I will be studying mice which have single knockout of either TFE3 or TFEB and double knockouts of both aforementioned proteins. I will be performing Luciferase assays in primary mouse naive CD4⁺ T cells to examine under what stimulatory conditions TFE3 and TFEB are needed for CD40L expression. I will also be comparing TFE3 and TFEB expression in a cohort of CD4⁺ T cells from healthy individuals and patients suffering from Systemic lupus Erythematosus (SLE).

TFE3 and TFEB have been shown to be involved in TGF β signaling pathway in non-lymphoid cells. It has also been shown that TGF β signaling is involved in the generation of regulatory/suppressor T cells (Tregs), which are involved in maintenance of immunologic homeostasis and control of self reactivity. Studies have shown that TGF β is essential for the generation of Forkhead box P3 (FoxP3) positive Tregs (inducibleTregs). Our lab has shown that mice expressing the TDN protein in T cells as well as mice lacking TFE3 are impaired in their ability to differentiate into FoxP3⁺ iTregs invitro. However mice lacking TFEB seem to have no impairment

Olipriya Das

Advisor(s): Richard Kollmar

The Role of the C1q Domain of Zebrafish Otolin 1a in Otolith Morphogenesis

Otolin1 is an extracellular matrix protein of otoliths ("ear stones" of fishes), and otoconia ("ear dust" of higher vertebrates). These acellular biominerals are essential for the sense of balance; dislodging results in the most common human balance disorder, benign paroxysmal positional vertigo. Otolin1 comprises of a collagen and a C1q domain, similar to atypical collagens VIII and X. We propose that Otolin1 forms a scaffold to which other otolith proteins, Ca²⁺ and CO²⁻ ions bind during otolith morphogenesis, with C1q trimers as hubs and collagen triple- helices as spokes. To test this model, we investigated whether the Otolin1 C1q domain is necessary and sufficient to form trimers and higher complexes in vitro.

The zebrafish Otolin1a C1q domain was expressed in bacteria either alone or fused to thioredoxin. Multimerization of affinity purified recombinant proteins was assessed by size-exclusion chromatography and gel electrophoresis. Under denaturing conditions, recombinant C1q proteins formed monomers and trimers, but not dimers or higher- order complexes. Under native conditions, they formed only higher-order complexes. In contrast, thioredoxin alone only appeared as a monomer.

Our results are consistent with the proposed ability of the Otolin C1q domain to form trimers that, in turn, assemble into higher-order complexes. Experiments are underway to characterize the various complexes in more detail and to test whether the C1q domain is necessary to trimerize of full-length Otolin1a.

Peiqi Ou

Advisor(s): Chongmin Huan

Sphingomyelin Synthase 2 deficiency impairs B cell apoptosis in the periphery and results in lupus-like disease

Systemic lupus erythematosus is an autoimmune disease characterized by anti-DNA antibodies produced in self-reactive B cells. It remains a clinical challenge due to a lack of effective treatments. Human and animal studies indicate that failed clearance of self-reactive B cells generated by somatic mutation in germinal centers is the major cause of the disease. Determining the mechanism of the checkpoint that eliminates self-reactive B cells in germinal centers is therefore important for designing therapeutic strategies for lupus. Sphingomyelin synthase 2 (SMS2) is a plasma membrane enzyme that catalyzes the synthesis of sphingomyelin while generating diacylglycerol as a by-product. We found that SMS2 deficient mice have increased numbers of peripheral B cells and production of anti-DNA autoantibodies that result in a lupus-like phenotype. Interestingly, activation of PKC δ , a key mediator of B cell checkpoints in both humans and mice, is defective in SMS2 deficient peripheral B cells. In this study, we identify SMS2 as a direct activator of PKC δ in peripheral B cells which prevents autoantibody generation. This discovery provides insights for the development of new diagnostic and therapeutic approaches.

Andre Valentin

Advisor(s): Chongmin Huan
Antonio E. Alfonso

REG1 Promotes the Development of Chemoresistance in Pancreatic Cancer Cells through Activation of AKT

Introduction: AKT is a major cell survival mediator in pancreatic cancer. Clarifying the mechanism of its activation in response to chemotherapy is desirable for designing strategies to overcome pancreatic cancer chemoresistance. Recently, REG3A was identified as an extracellular activator of AKT in psoriatic keratinocytes. This finding implies that AKT in pancreatic cancer cells could be activated by REG1, a REG3A family member, which is mainly secreted by acinar cells and has promoting effects on pancreatic cancer. Furthermore, we found that in pancreatic cancer cells, gemcitabine treatment significantly increased expression of EXTL3, a receptor shared by REG1 and REG3A. Therefore we hypothesize that acinar cell-derived REG1 promotes the development of chemoresistance in pancreatic cancer. In this study, we investigated REG1-mediated gemcitabine resistance in Panc-1 and MIA-paca-2 pancreatic cancer cells.

Methods: EXTL3 expression in gemcitabine-treated cells was evaluated by Western blot and RT-PCR. REG1-induced activation of AKT and AKT-regulated p21Cip/Waf1 cellular location were analyzed by Western blot and immunofluorescence staining respectively. Survival of gemcitabine-treated cells with/without REG1 stimulation and AKT inhibition was quantified by measurement of cellular dehydrogenase activity.

Results: REG1 supplementation significantly increased AKT phosphorylation and AKT-mediated cytoplasmic location of p21Cip/Waf1 in cultured pancreatic cancer cells. These effects resulted in the enhanced resistance to gemcitabine that could be reversed by AKT inhibition.

Conclusion: REG1 is an AKT activator that increases chemoresistance in pancreatic cancer cells, suggesting an adverse role of acinar cells during pancreatic cancer chemotherapy. Targeting REG1 to overcome chemoresistance is being investigated in our REG1 deficient orthotopic mouse model of human pancreatic cancers.

Ankuri Desai

Advisor(s): Edward Quadros

A rat model for folate receptor antibody-mediated behavioral deficits: Implications of folate receptor autoantibodies in autism

This study examines the role of antibodies against the folate receptor alpha (FR α) on brain development and function to determine if a similar mechanism could operate in autism spectrum disorders (ASD) and other neurodevelopmental disorders. A previous study in our laboratory found that >70% of children with ASD are positive for serum FR-autoantibodies. Consequently, we developed a rat model to study the behavioral and cognitive deficits induced by exposure to FR-antibody during gestation and weaning. We focused particularly on behavioral deficits that mirror those seen in ASD. We studied the transfer of FR-antibodies from mother to fetus and identified regions of the brain affected most by this antibody accumulation, which could potentially lead to the identification of regions involved in the functional and behavioral changes seen in ASD. Effective interventions to help in the treatment of those with ASD and FR-antibodies were considered, looking specifically at the efficacy of folic acid and dexamethasone in preventing the behavioral deficits induced by FR antibodies in the rat model.

Our results demonstrate that rats exposed to FR antibodies during gestation or weaning display core ASD symptoms such as deficits in communication, socialization, and set-shifting tasks. They also have learning and memory deficits. Treatment with folic acid and dexamethasone results in significant improvement of the deficits. FR antibody exposure during gestation decreases folate transport from mother to fetus with antibody localizing to embryo, placenta, uterine wall, yolk sac, and amnion. Overall, these studies were aimed at understanding the effect of FR antibodies on fetal and infant brain development and function. The outcome of these studies could herald a paradigm shift in our understanding of ASD and other developmental disorders associated with FR autoimmune disorder.

Sean Mahase

Advisor(s): David Zagzag

A novel CXCR4 antagonist inhibiting glioma cell migration suggests its clinical utility against gliomas' evasive resistance to antiangiogenic therapy

Background: Human glioblastoma (GBM) are highly vascularized malignant tumors that are candidates for antiangiogenic therapies, e.g., the anti-vascular endothelial growth factor (VEGF) antibody bevacizumab (BEV), directed against VEGF overexpression by tumor cells. A majority of patients eventually developed resistance to BEV as evidenced by intracerebral dissemination of glioma associated with tissue hypoxia known to promote invasion. Because BEV may promote glioma invasion through hypoxia-induced expression of the chemokine receptor CXCR4 on invading tumor cells and their migration towards brain neurons and blood vessels expressing its ligand stromal cell-derived factor (SDF)-1 α , we hypothesized that inhibition of CXCR4 may blunt glioma invasion. In collaboration with Polyphor Ltd. (Switzerland) that has developed selective, highly potent CXCR4 antagonists, e.g., POL5551, we showed that mouse glioma models treated with a BEV analog in vivo emulated the invasive phenotype seen in human GBM but that combined therapy with POL5551 greatly reduced tumor invasiveness. To confirm these results in vitro, we performed glioma cell migration and cytotoxicity assays with POL5551.

Methods: Murine glioma cells were seeded onto Boyden chamber filters with a variable dose of POL5551 and incubated in the presence of a SDF-1 α gradient under normoxic or hypoxic (1% O₂) conditions. After 24 h, the filters were fixed, stained with toluidine and the number of migrated cells counted. To exclude cytotoxic effects by POL5551, the viability of glioma cells exposed to a variable dose of POL5551 was assessed after 24 h using a tetrazolium dye reduction assay.

Results: Under normoxic and hypoxic conditions, the migration of glioma cells increased in the presence of SDF-1 α , but was significantly curtailed by POL5551. No evidence of cytotoxicity of POL5551 was detected.

Conclusions: Our results support the potential clinical utility of CXCR4 antagonists as adjunct therapy for patients with GBM.

Megan Maraynes

Advisor(s): Jennifer Chao
Richard Sinert, Shahriar Zehbtachi, Konstantinos Agoritsas

Screening for Asymptomatic Chlamydia and Gonorrhea in Young Males in an Urban Emergency Department

BACKGROUND: Chlamydia Trachomatis (CT) and Neisseria Gonorrhea (GC) are the most common bacterial sexually transmitted infections (STI) among sexually active adolescents. Both CT and GC are frequently asymptomatic in males. Little is known about the prevalence of asymptomatic STI in adolescent males. Adolescents do not utilize primary care frequently, and are often seen for acute issues in the emergency department setting, thus minimizing screening opportunities.

OBJECTIVE: To determine the prevalence of asymptomatic CT and GC in young men seeking care in the emergency department (ED) for non-STI related symptoms. **DESIGN/METHODS:** Prospective, cross-sectional pilot study in an urban ED. Inclusion criteria: males age 16-21 presenting with non-STI related complaints. Exclusion criteria: genitourinary or STI-related complaints at triage, current antibiotic therapy, and high acuity level (Emergency Severity Index 1-3). **Outcome:** rate of positive CT and GC. After informed consent, patients were tested for CT and GC via urine RNA assay. Data are presented as medians with quartiles for continuous variables and as percentages with 95% confidence intervals for proportions. **RESULTS:** 249 patients were included (age range 16-21, median: 18 [quartiles 16-18, 19-21]). Overall, 7% (95% CI, 4-11%) tested positive for CT and 0% (95% CI, 0-2%) were found to have GC. The overall proportion of sexually active subjects was 76% (95% CI, 70-80%), and 2% (95% CI, 0.7-4%) reported sex with men. Previous STI testing was reported in 50% (95% CI, 44-56%) of enrolled subjects, and 6% (95% CI, 4-11%) of all patients had a history of positive STI results. Of the patients who tested positive for CT in the ED, 82% (95% CI, 58-95%) were successfully followed up and treated.

CONCLUSIONS: The relatively high rate of CT infection found by screening justifies routine STI screening in young adolescents presenting to the ED with non-STI related complaints.

Nishit Patel

Advisor(s): Jennifer Chao

The Practice of Obtaining a CXR in Pediatric Patients Presenting With Their First Episode of Wheezing in the ED: A Survey of Attending Physicians.

Background: Routine use of CXR in pediatric patients presenting with their first episode of wheezing was recommended. Although recent studies conclude that a CXR is not routinely indicated in these children, there continues to be reports of overuse.

Objective: To identify the current practice and factors that influence obtaining a CXR in pediatric patients presenting with their first episode of wheezing to an ED in the USA.

Methods: The 14-item survey targeting attending ED physicians who see children with wheezing, was distributed electronically to the nearly 3,000 members of the PEM Brown listserv and the American College of Emergency Physicians listserv. Data were analyzed using descriptive statistics and Chi-square test.

Results: Of the 537 physicians who participated, their primary residency training was: 42% pediatrics, 54% emergency medicine and 4% other. 72% of participating physicians supervise residents, 54% were board eligible or certified (be/bc) in PEM. 30% (95% CI: 26-34) of participants indicated that they would always obtain a CXR in pediatric patients presenting with their first episode of wheezing. 81% (95% CI: 75-87) of those who always obtain a CXR believe that it is standard of care. Of the 376 physicians who do not always obtain a CXR, 18% (95% CI: 15-23) always obtain a CXR under certain age (2 weeks to 12 years, median of 1 year). Physicians who report a primary residency in pediatrics, supervise residents, be/bc in PEM, and practicing for greater than 5 years were less likely to obtain a CXR ($p<0.001$, $p<0.001$, $p<0.001$, $p=0.006$).

Conclusions: 30% of physicians routinely obtain a CXR in first time wheezer. The factors influencing this practice are primary residency training, fellowship training, resident supervision, and years of independent practice. This identifies a target audience that would benefit from education to decrease the overuse of CXRs in pediatric patients with wheezing.

Elna Kochummen

Advisor(s): Vivian Chin

A Rare Case of Bilateral Hurthle Cell Adenoma in an Adolescent

Hurthle cell neoplasms are rare among pediatric thyroid cancers. Hurthle cell adenoma (HCA) rarely present bilaterally while Hurthle cell carcinoma (HCC) can be bilateral and invasive, necessitating total thyroidectomy. We report a case of an adolescent with bilateral HCA.

Case: 14 year old healthy female presented with painless, non-progressive neck swelling and no other symptoms for 1 month. Her thyroid measured 4.5 cm and 6 cm on the right and left lobes respectively. TSH was low (0.20 uIU/mL) and free T4 normal; thyroid antibodies were normal. Ultrasound (US) revealed three small nodules in the right lobe; a large nodule occupied the majority of the left lobe with solid and cystic areas with hypervascular flow and no microcalcifications. Fine Needle Aspiration Biopsy (FNAB) was negative for malignancy. One month later, she had worse neck swelling and dysphagia. Exam showed a nontender nodule measuring 2x3 cm on the left. Labs and US were unchanged. 14 months later, the patient returned with worse neck swelling, dysphagia, and hyperthyroid symptoms but was euthyroid. CT scan revealed an oval heterogeneously enhancing mass in the left lobe with mild tracheal deviation to the right. Left hemithyroidectomy confirmed a diagnosis of HCA. By one year post-op, a nodule in the right lower pole doubled in size and increased in vascularity. FNAB was nondiagnostic. Right hemithyroidectomy revealed HCA.

Conclusion: HCA represent benign localized growth, unilateral involvement and non-recurrent behavior. Distinction between HCA and HCC is important due to the highly aggressive nature of HCC. Diagnosis relies upon surgical histopathology because FNAB fails to differentiate between the two. Vascular/capsular invasion or metastasis support a diagnosis of HCC. To our knowledge, this is the first case of bilateral HCA in an adolescent. This case highlights the importance of histopathology in the assessment of thyroid nodules and the variability in biological behavior of HCA.

Jeffrey Tan

Advisor(s): Kay Beharry
Douglas R. Lazaro, Jacob V. Aranda

Long-Term Ocular Adverse Effects of Intravitreal Avastin in a Rat Model of Oxygen-Induced Retinopathy

Introduction: Using an established animal model for oxygen-induced retinopathy (OIR) we hypothesized that the effects of Avastin are dependent on the oxygen environment and that local and systemic adverse effects of Avastin are potentiated by intermittent hypoxia (IH).

Methods: Neonatal rats at birth were exposed to hyperoxia (50% O₂) or intermittent hypoxia (50% O₂ with brief episodes of hypoxia (12% O₂) from P0-P14. At P14, the time of eye opening, a single dose of Avastin (0.125 mg in 0.005 mL) was injected into the vitreous cavity of the left eyes. Room air (RA) littermates served as oxygen controls and saline served as vehicle controls. At P23 and P45 (pubertal, mating) blood gases, somatic growth, ocular angiogenesis, retinal pathology, and ocular and systemic biomarkers of angiogenesis (VEGF, sVEGFR-1, & IGF-I) were examined.

Results: Avastin use was associated with long-term elevations in PCO₂, and reduced body weight accretion, predominantly in the RA groups. Treatment with Avastin in IH resulted in the most profound effects with robust rebound increases in systemic and ocular VEGF at P45, although no reciprocal somatic growth was noted. Similar elevations in choroidal IGF-I levels occurred with Avastin treatment in IH, which was also evident in the untreated, fellow eyes. Avastin decreased systemic and retinal sVEGFR-1 at P45 in the groups exposed to IH. The retinal flat-mounts showed decreased peripheral vascular growth in both treated and untreated eyes at P23, but at P45, there was evidence of pathologic vascularization with Avastin treatment in IH. Histological analysis showed induced retinal damage particularly in the inner and outer plexiform layers.

Conclusion: The adverse effects of Avastin in rat pups are highly potentiated in intermittent hypoxia, and these findings should be considered when intravitreal Avastin use is entertained in human neonates, especially in those that are extremely pre-term.

Danielle Joseph

Advisor(s): Stacy Blain

The Plasticity Potential of the Putative Multiple Myeloma Cancer Stem Cell

Multiple myeloma (MM) is characterized by a clonal proliferation of the plasma cell within the bone marrow. Patients with this malady may undergo chemotherapy and autologous stem cell transplant yet relapse is inevitable. This suggests that the current treatment regimens are ill-targeted and there are MM cells that exhibit stemness characteristics that enable them to evade chemotherapy and reinitiate tumor growth. Stemness is defined by four characteristics: the ability to self-renew, to differentiate, to remain in a slowly proliferating or quiescent state and to be chemoresistant. Previous data proposes that the MM cancer stem cell is the CD138- pre-plasma cell because it exhibits these qualities. However, our data unexpectedly demonstrates that the CD138+ tumor cell may also be able to dedifferentiate into its precursor regaining the qualities of stemness. As this happens in culture in the absence of supportive accessory cells, we believe that cytokines produced by the CD138+ cell are responsible for its plasticity. We analyzed the secretion of 31 different cytokines and have been able to identify cytokines produced by both populations, which may contribute to their differentiation status. We identified MIF-1, IL-16, CXCL10, Serpin E1, and GM-CSF. MIF-1 in particular has been implicated in MM cell adhesion to BM. We aim to characterize the CD138- cell further and determine the link between differentiation and the autocrine cytokine loop of the CD138+ cell. Our data suggests that certain signal transduction pathways are responsible for this plasticity. Targeting these pathways may demonstrate that blocking this interconversion will alter chemosensitivity. Our data implies that the notion of a phenotypically defined cancer stem cell in MM may not be applicable. This project has important clinical implications because it suggests that any MM tumor cell that escapes chemotherapeutic assault, may have the potential to reacquire stemness and reinitiate tumor growth.

Priyank Patel

Advisor(s): Stacy Blain
Ameer Hassoun

Alt Brk, an inhibitor of p27 phosphorylation, synergizes with Pablociclib to potently arrest breast cancer cells in G1 phase of the cell cycle

The oncogenes Cyclin D and cdk4 (D-k4) enhance the proliferation of cancer cells and Cyclin D is overexpressed in 80% of breast cancers. The D-k4 complex phosphorylates the gate keeper pRb promoting the G1-S phase progression of the cell cycle. p27 is required to assemble and activate the complex. Depending on the phosphorylation state of its Tyrosine (Y) 88 and 89 residues, p27 can inhibit or activate the complex. When Y88 and Y89 residues are phosphorylated, p27 vacates the ATP binding pocket of cdk4, permitting catalytic activation of the D-k4 complex. Since it serves as an ON/OFF switch for the D-k4 complex, we wanted to find the physiological kinase that phosphorylates p27, and identified Breast Tumor Related Kinase (Brk). Brk interacts with p27 via a classical SH3:PxxP interaction, which can be blocked by small peptide of either the Brk SH3 domain or p27's PxxP domain. A catalytically inactive alternative spliced variant of Brk, Alt Brk, which consists of only the SH3 domain, is expressed in breast cancer cells. Alt Brk competitively binds to p27kip1, preventing Brk's phosphorylation of p27 and inhibiting activation of D-k4. Expression of Alt Brk in the breast cancer cell line MCF7 inhibited p27 phosphorylation and switched the activity of D-k4 'OFF'. Recently, a cdk4 specific small molecule inhibitor, Pablociclib, was approved for clinical use. We found that expression of Alt Brk in MCF7 cells caused a potent G1 phase arrest. Alt Brk blocks p27 Y phosphorylation, which may inhibit cdk4 and reduce p27's degradation, allowing it to inhibit cdk2 as well, making it a better cell cycle inhibitor. Alt Brk also synergized with Pablociclib to arrest the cell cycle more potently than either therapy alone and provided a more durable arrest than Pablociclib treatment. In summary, our data suggest that a p27 phosphorylation inhibitor might be an effective way to arrest cancer cell proliferation.

Elina Shteyn

Advisor(s): Stacy Blain

Establishing the Role of Brk in Pancreatic Cancer.

The cyclinD-cdk4 complex inactivates the Rb-dependent G1 checkpoint and allows progression of the cell cycle from the G1 to S phase. p27 acts as an on/off switch for cyclinD-cdk4 activity. Breast tumor kinase (Brk) phosphorylates p27 at Y88 (pY88) to relieve its inhibition on the cyclin D-cdk4 complex. Deregulation of cdk4 activity leads to the loss of control of the G1 checkpoint. Data suggests that abnormal cdk4 activity might contribute to the development of pancreatic ductal adenocarcinoma (PDAC).

Here, we examined the role of Brk in pancreatic cancer cells. We treated six pancreatic cell lines derived from different tumor grades with Palbociclib, a cdk4 specific inhibitor. These cell lines have mutated Ink4a (the endogenous cdk4 inhibitor) and active K-RAS, suggesting that constitutively active cdk4 drives proliferation. Surprisingly, we detected two classes of cancer cells: a sensitive group with IC50 values ranging from 1 μ M - 2.3 μ M and a resistant group with IC50 values ranging from 9.8 μ M -25.7 μ M. Western blot analysis did not show any significant differences in the protein levels of the G1 cell cycle players between the sensitive and resistant lines. However, we saw much higher levels of Brk in the resistant lines as compared to the sensitive lines. Furthermore, immunofluorescence and immunoprecipitation studies show that the levels of pY88 correlated with the levels of Brk in all cell lines. Thus, both results suggest that resistant cell lines might have upregulated Brk leading to an increase in cyclinD-cdk4 activity that could not be inhibited by Palbociclib. We will perform kinase assays on the panel of the pancreatic cell lines to test the correlation between cdk4 activity, Brk, p27 pY88 and resistance to Palbociclib, with the goal of determining whether these markers could be used to identify tumors that would respond to this treatment.

Sandra Carvajal-Raga

Advisor(s): Tamar Smith-Norowitz

Jeremy Weedon, Rauno Joks, Kevin B Norowitz, Diana Weaver, Helen G Durkin, Margaret R Hammerschlag, Stephan Kohlhoff

Increased seroprevalence of anti-Enterovirus 71 IgE antibodies in asthmatic compared with nonasthmatic children.

Background: Asthma is a common pediatric chronic inflammatory airway disease worldwide, with increasing prevalence. Respiratory viral infections are frequent infectious triggers for exacerbations of asthma

Objective: To determine whether enterovirus 71 (EV71), a ubiquitous virus that causes systemic inflammatory responses in children but is not a known respiratory pathogen, can also serve as an infectious trigger for asthma.

Methods: We measured specific anti-EV71 IgE and IgM antibodies (Ab), total serum IgE, and IL-2 and IL-4 cytokine levels in serum of asthmatic and non asthmatic children. Data are expressed as median [interquartile range] with 2-tailed Mann-Whitney test p-values.

An analysis of covariance was conducted on log-10-transformed IgE and IgM anti-EV71 scores, with predictors asthma status and age

Results: Asthmatic children had higher IgE anti-EV71 Ab levels than non asthmatic children .Non-asthmatic children had significantly higher IgM anti-EV71 Ab levels than asthmatic children .Interestingly, despite the relatively low serum IgE levels of non-asthmatic, compared with asthmatic children , the nonasthmatic children produced significantly more IL-2 and IL-4 than asthmatic children The ages of the asthmatics, but not the nonasthmatics had a significant effect on the levels of IgE anti-EV71. A test of difference between these two slopes was statistically significant . However, the ages of the nonasthmatic, but not the asthmatic children had a significant effect on the levels of IgM anti-EV71A test of difference between these two slopes was statistically significant .

Conclusion: Increased specific anti EV71 IgE responses may indicate that EV71 infection may also be an infectious trigger in asthma. However, the role of specific anti-EV71 IgM, Th2 cytokines, and age in non-asthmatic children should be further studied

Shipra Bansal

Advisor(s): Sheila Perez-Colon

Knowledge, Attitudes and Practices of US residents regarding insulin pump in diabetics

Background: Insulin pump (IP) use is increasing due to improved glucose control in diabetics. These patients present to inpatient, outpatient and ER settings for treatment, hence, hospital staff needs to have basic knowledge of IP. Residents (RES) may need to look up or change settings on IP. Also, as independent providers after training, they may encounter patient on the IP at their offices.

Objective: To assess the Knowledge, Attitudes and Practices of RES in USA regarding IP in DM patients.

Design/Methods: Cross-sectional study. After IRB approval, emails were sent to all Pediatrics (PED) and Internal Medicine (IM) Program Directors or Coordinators in USA to be forwarded to their RES with the link to an online anonymous questionnaire. Reminder email was sent after 2 weeks. Frequency tables, ANOVA, t-test ($p < 0.05$ significant) were used for data analysis.

Results: Out of 314 responders, 93 - PGY1, 102- PGY2, 106- PGY3 and 10 -PGY4 while 3 did not answer this question. Specialty (SPL) wise, 182 were PEDS, 91 IM and 21 were combined Medicine-Pediatrics RES while 20 chose not to reply. 42% had done at least one endocrine rotation (ROTATION). 194 RES saw 1-2 diabetics per month on IP, 15 saw >3 while 100 of them saw none.

The mean knowledge scores (KS) significantly improved ($p=0.005$) with the training level and doing ROTATION ($p<.0001$). No significant differences in KS were noted based on the SPL or number of diabetics seen. 40% of 292 believe that IP use does not increase the risk of DKA from pump malfunction or allows precise insulin delivery compared to a syringe. $<50\%$ of 284 RES were confident in looking up or changing IP settings. 70% RES feel that they lack experience during their training for IP and wish to learn more about it.

Conclusions: Despite adequate knowledge among some RES about IP, there is a need for improvement in their attitudes and practices. It is vital that RES get training about it as it is an effective form of insulin delivery.

Rafael Flores-Obando

Advisor(s): Charles Abrams

The role of mutations in connexin47 (Cx47) in myelinating cells of the central nervous system (CNS)

Connexin47 (Cx47) forms homotypic gap junction communication channels between oligodendrocytes (OLs), the myelinating cells of the CNS and forms heterotypic channels with Cx43 in astrocytes. Pelizaeus-Merzbacher-like disease 1 (PMLD1) arises in patients with mutations in GJC2 -encoding Cx47- causing nystagmus, cerebral ataxia, and spasticity within the first 6 years of life. One mutation (p.Ile33Met) has been associated with a much milder phenotype, hereditary spastic paraplegia type 44 (SPG44). In cell lines, PMLD1 mutants such as Cx47P87S cause defective protein trafficking, endoplasmic reticulum (ER) retention and loss-of-function. These studies have not been conducted in OLs, where ER retention of Cx47P87S could lead to cell type-specific cellular stress, activation of unfolded protein response (UPR) pathways and apoptosis. We hypothesize that mutations in Cx47 associated with severe phenotype (Cx47P87S) cause toxic gain of function compared to the milder Cx47I33M mutation. We have optimized the isolation and culture of primary OLs from neonatal Cx47 knockout mice pups using immunomagnetic beads. OLs were lentivirally transduced to express Cx47WT and mutants. Using immunofluorescence (IF) studies we show that Cx47P87S exhibited a diffuse cytoplasmic staining compared to the puncta staining of Cx47WT and Cx47I33M. Also, IF staining for Cx47 and ER resident chaperone Grp94 showed that Cx47P87S staining colocalized with Grp94 compared to Cx47WT and Cx47I33M. Finally, IF staining for C/EBP homologous protein (CHOP) -a component of the UPR mediated apoptosis pathway- and ZsGreen -a reporter of lentiviral transduction- showed an increased CHOP activation in OLs expressing Cx47P87S compared to Cx47WT and Cx47I33M. These results indicate that in primary OLs Cx47P87S protein, but not Cx47I33M, is retained in the ER and activates the UPR pathway. Ongoing studies will determine if the activation of the UPR pathway induces apoptosis in primary OLs expressing Cx47P87S.

Carrie Poon

Advisor(s): Frank Barone

Thrombopoietin Intervention After Stroke Injury Restores Sensory, Motor, and Cognitive Functioning in the Rat

Stroke is a major cause of death and can result in long-term sensory, motor, and cognitive deficits. Only 5% of stroke patients are able to meet the 4-hour time window for tissue plasminogen activator (tPA), the only current FDA approved treatment for stroke. Our lab has previously shown thrombopoietin (TPO), a hematopoietic platelet growth factor, has acute protective effects. When administered up to 4 hours after stroke (middle cerebral artery occlusion; MCAO) ischemic hemispheric swelling (edema) and infarction, inflammatory cytokines and blood brain barrier injury were significantly decreased. Sensory-motor coordination performance also improved. Here we investigate the effects of delayed treatment and long term outcome of TPO intervention. Male sprague-dawley rats underwent 2 hours of MCAO and were studied for 4 weeks for long term effects of TPO administration. Rats received 2 intravenous injections of either phosphate buffered saline (PBS) or TPO (0.1ug/kg; optimal dose). The first injection was administered 1 day after MCAO (when the infarct is fully developed) and the second dose was administered 4 days after MCAO. Neurological deficits at 4 weeks improved significantly in TPO-treated group compared to PBS-treated group. In the active place avoidance task to test cognitive abilities, TPO treated group received fewer shocks with fewer entrances and were able to avoid the shock zone whereas the PBS group could not. Immunohistochemical measurements using CD31 showed that TPO improved behavioral outcome was associated with an increase of microvessels in the cortical peri-infarct region 4 weeks post-stroke. TPO increased peri-infarct angiopoietin-1 at 2 weeks post-stroke. Ongoing immunohistochemical studies are investigating VEGF expression at 1 and 2 weeks post-stroke. MRI arterial spin labeling and vascular integrity measurements will also be done to understand peri-infarct blood flow and vascular integrity associated with TPO-induced microvessels.

Johnson Ho

Advisor(s): Peter Bergold
Michael Sangobowale

Minocycline and N-acetylcysteine modulates inflammatory response in a mild closed-head injury mouse model of traumatic brain injury.

Traumatic brain injury (TBI) causes structural and functional deficits due to complex neurodegenerative disease mechanisms that evolve over minutes to months after injury. A single blunt impact to adult C57/BL6 mice produces two injury syndromes (CHI-1 and CHI-2) that are distinguished by their breathing status and recovery of righting reflex immediately after impact. High-speed image capture of a single closed-head impacts revealed that a single closed-head impact produced similar head displacements, but significantly different peak vertical acceleration and deceleration amplitudes. Despite the control of impact parameters, TBI models that allow for head movement have inherent heterogeneity. The assessment of acceleration-deceleration amplitude is an additional parameter that determines severity of brain injury. Head movements also correlate with immediate physiological response after impact and likely cause the subsequent histological injury and behavioral deficits.

The role of neuroinflammation following TBI is poorly understood. Treatment of either rats or mice with minocycline and N-acetylcysteine (MINO plus NAC) produces large-scale structural and behavioral improvements following TBI. Mechanisms underlying these improved outcomes are unknown. Acute neuroinflammation following TBI may also promote important protective and regenerative effects. This project investigated how MINO plus NAC modulated neuroinflammation following TBI. Post-injury neuroinflammation was assayed using inducible nitric oxide synthase (iNOS), a marker for pro-inflammatory M1 microglia, and microglial activation was assayed using Iba-1. iNOS expression by microglial cells following TBI was further increased by MINO plus NAC treatment 2 days after injury. This increased expression suggests that MINO plus NAC rapidly reformats the microglial response to brain injury. This alteration of microglial activation may underlie some of the therapeutic effects of MINO plus NAC.

Elena Nikulina

Advisor(s): Peter Bergold
Michael Sangobowale, Johnson Ho

Minocycline and N-acetylcysteine enhance astrogliosis early after experimental traumatic brain injury and improve survival of hippocampal neurons.

Treating animals with combination of minocycline (MINO) and N-acetylcysteine (NAC) alleviates behavioral deficits in mouse closed-head injury (CHI) model. MINO plus NAC preserves myelin in the Cingulum, Fimbria and Corpus Callosum. Combination of MINO and NAC modulates also microglial activation. Microglia and astrocyte activation are interdependent and mutually-enhancing, so we investigated whether the treatment changes the dynamics of reactive gliosis as well, and if it correlates with better axonal preservation in the mouse CHI model. Depending on its activation state, reactive astrocytes may be detrimental or protective after CNS injury. In experimental models other than TBI, reactive astrocytes increase the release of neurotrophic factors, enhance energetic supply, enhance glutamate uptake, thereby increasing the chances of neurons to survive and to repair axonal damage, which, in turn, may improve the survival of oligodendrocytes and promote functional re-myelination.

Our preliminary results indicate MINO plus NAC accelerates reactive gliosis. In MINO and NAC-treated injured mice, we observed enhanced astrocytes activation in Hilus, Splenium and Fimbria at 2 days post lesion (DPL) as compared to injured mice treated with saline. In contrast, at 14 DPL GFAP upregulation is more prominent in saline-treated injured mice. Thus, early astrocytes activation correlates with improved survival of hippocampal hilus neurons and sparing of white matter tracts. Hippocampal hilus neurons are selectively vulnerable in several neurodegenerative conditions and in neurodegeneration animal models. It has been demonstrated in the lab previously that MINO plus NAC modulate microglia activation and preserve oligodendrocytes. Now we show that treatment changes the dynamics of astrogliosis and preserve axonal tracts. Overall, these data support the notion that enhanced neuroinflammation early after injury improves brain repair after traumatic injury.

Michael Sangobowale

Advisor(s): Peter Bergold

MINO plus NAC limits a heterogeneous TBI injury within a clinically useful therapeutic window

The inherent heterogeneity of TBI (traumatic brain injury) has been a barrier to finding effective therapies. To better model the heterogeneity of TBI, we report a closed head injury (CHI) experimental TBI that reliably produces two injury syndromes (CHI-1 and CHI-2) after a single closed head impact to adult mice. CHI-1 and CHI-2 mice differ in righting reflex, and cognitive and memory deficits. White matter injury was assessed in cerebellum, cingulum, corpus callosum, fimbria and splenium 14 days after an initial MINO plus NAC dose 1 hour after injury. Myelin was assayed using luxol fast blue and axon density measured using a pan neurofilament antibody. CHI-2 mice had widespread myelin and neurofilament loss in cerebellum, cingulum, corpus callosum, and fimbria. 14 days after injury, mice treated with MINO plus NAC increased luxol staining in the cingulum, fimbria, and corpus callosum. At 14 days, CHI-2 mice show a significant loss of MAP2 and NeuN immunoreactivity in the hilus, CA3 and CA1 regions. No change was observed in the granule cell layer of the dentate gyrus at 14 days. The more widespread grey and white matter damage in CHI-2 correlates with the more severe behavioral deficits. MINO plus NAC also shows drug efficacy when dosed 6 hours after injury. Thus, MINO plus NAC maybe an effective treatment for the inherent heterogeneity of clinical TBI.

Peng Gao

Advisor(s): Joseph Francis
Alejandro Iván Hernández, Jeffrey Goodman

Changes of PKM ζ Expression in the Sensorimotor Cortex of Adult Rat After Motor Learning

Previous studies have suggested that motor learning could induce neuroplasticity changes in the sensorimotor cortices. For example, the level of long-term potentiation (LTP), a widely used cellular model for the study of learning and memory, was modified after a skilled reaching task in the sensorimotor cortex of adult rat. Meanwhile, the inhibition of protein kinase M ζ (PKM ζ), which is necessary and sufficient for the maintenance of LTP, disrupted the learned sensorimotor memories. In this study, we investigated the changes of PKM ζ expression in the sensorimotor cortex of adult rat after a skilled reaching task. Our goal is to better understand the molecular mechanisms that construct, modify, and maintain neural circuits for motor learning.

John Hessburg

Advisor(s): Joseph Francis

Comparison of single-unit and multi-unit response in M1 to rewarding and non-rewarding trials

The ability to accurately discriminate neural activity is essential to the development of brain machine interfaces (BMIs). Current recording methods record data from a number of neurons, which then must be sorted into their constituent parts. In this study non-human primates (NHPs) were trained to conduct a center-out reaching task in which they were rewarded with a liquid juice reward for successfully reaching and holding at the target. Motor cortex activity was recorded as the animal performed the task, and the reward delivery was varied such that there were trials when the animal expected a reward and then received it, and others where the animal did not receive the expected reward. The activity was sorted using a semi-automated offline sorter to differentiate units. The activity was also sorted using an unsupervised wavelet transform and superparamagnetic clustering with the goal of obtaining single-unit activity (SUA). This SUA was compared to the multi-unit activity (MUA), to determine if breaking down recorded data to this level was necessary for future analysis and implementation of BMIs.

David McNeil

Advisor(s): Joseph Francis

Comparison of Classification Methods for Predicting Reward in Primary Somatosensory Cortex

Rewarding stimuli are known to cause neural modulation within many structures of the brain. Although these signals were first described in relation to the delivery of a food or liquid reward, they have also been shown to exist in response to a myriad of stimuli. Classification of rewarding versus non-rewarding stimuli was performed on data collected from the primary somatosensory cortex of a primate during performance of a reaching task. Following successful completion of a given trial the animal was either rewarded with juice or given no reward. Using binned neural data following the delivery of reward for each trial as features, several classifiers were used to classify a trial type as rewarding or non-rewarding. Classification of single trials as either rewarding or non-rewarding yielded an area under the receiver operating characteristic (ROC) curve ranging from 0.53 to 0.94 depending on the classifier type implemented. Control data analyzed in the same fashion yielded an area under the ROC curve ranging from 0.50 to 0.60.

Rachelle Dugue

Advisor(s): Douglas Ling

The Effect of the Calpain Inhibitor Gabadur on Traumatic Brain Injury

Traumatic brain injury is a leading cause of chronic disability; it afflicts people of all ages with over 1.7 million traumatic brain injuries occurring per year. A successful treatment to stop the progression of traumatic brain injury and prevent the consequent neurological and functional deficits has not yet been determined. Gabadur is a novel calpain-inhibitor therapeutic derived from the protease inhibitor leupeptin linked to the FDA-approved drug, pregabalin, as a carrier molecule. This combination permits the compound to cross the blood brain barrier after peripheral administration and potentially has a dual therapeutic effect.

We hypothesize that the administration of Gabadur can halt calpain over-activation post-injury and reduce neurological and functional deficits that occur following severe traumatic brain injury.

80 mg/kg of Gabadur was administered immediately following injury induced by the controlled cortical impact rodent model of traumatic brain injury. In comparison to control rats given phosphate buffered saline (PBS), rats given Gabadur immediately following severe traumatic brain injury displayed a significant reduction in the number of degenerating cortical neurons, as shown by Fluoro-Jade B staining ($p < 0.05$). A decrease in the amount of calpain-mediated α II-spectrin breakdown product was also observed in comparison to control rats given PBS ($p < 0.05$). Microglia and glial fibrillary acidic protein (GFAP) were analyzed in Gabadur-treated versus control, PBS-treated groups.

Anna Bulanova

Advisor(s): William Lytton
Michael Hines, Yale School of Medicine

Integrating Systems Biology Markup Language (SBML) with NEURON

The NEURON simulator software is widely used by the computational neuroscience community for electrophysiology modeling. Many reaction simulations, written for a variety of different cell types in various organs, have been developed in the Systems Biology Markup Language (SBML), a standard XML-based format supported by over 200 software packages. We introduce SBML support for NEURON, which enables NEURON users to import previously developed cell biology models and use them in computational neuroscience research. These can then combine with NEURON's electrophysiological simulation capabilities, and with other intracellular reaction models written in the new RxD syntax. This allows combined use of 2 extensive collections: the neuroscience ModelDB (<http://senselab.med.yale.edu/modeldb/>) and the SBML BioModels (<http://www.ebi.ac.uk/biomodels-main/>) databases.

Import and export of SBML models is handled using the libSBML library. A critical feature is a method to match state variables across the different models and different modeling levels. We also give the user facilities to make sure that semantically identical parameters are identified across models and to manage parameters, regardless of their origin.

We demonstrate new syntax by creating a new model using existing models from ModelDB and BioModels databases.

The importation procedure is as follows: 1) an electrophysiology model is loaded from ModelDB or constructed de novo; 2) NEURON loads SBML model descriptions (and creates corresponding SBMLModelComponent objects) 3) the user identifies semantically identical names across the component model name spaces; 4) Diffusion constants are associated with appropriate SBML states; 5) appropriate RxD objects (rxd.Region, rxd.Species, rxd.Reaction) are instantiated; 6) the user adjusts parameters and makes simulation runs of the model.

We also show results of SBML conformance testing using SBML test suite available on <http://sbml.org>.

Salvador Dura-Bernal

Advisor(s): William Lytton

Restoration of behavioral performance via neural stimulation after simulated lesion in a cortical spiking network model driving a virtual arm.

Neural stimulation can be used as a tool to elicit natural sensory stimuli or motor behaviors by modulating neural activity. This can be potentially used to mitigate the damage of brain lesions or neural disorders by compensating for the perturbed activity. However, in order to obtain the optimal stimulation sequences, it is necessary to develop neural control methods, for example by constructing an inverse model of the target system. For real brains, this can be very challenging, and often unfeasible, as it requires repeatedly stimulating the neural system to obtain enough probing data and depends on an unwarranted assumption of stationarity. By contrast, detailed brain simulations provide an alternative testbed for understanding the interactions between ongoing neural activity and external stimulation. Unlike real brains, the artificial system can be probed extensively and precisely.

Here we employed a spiking network model of sensorimotor cortex trained to drive a realistic virtual musculoskeletal arm to reach a target. The network was then perturbed, in order to simulate a lesion, by either silencing neurons, or removing synaptic connections. All lesions led to significant behavioral impairments during the arm reaching task. The remaining cells in the system were then systematically probed with a set of single and multiple-cell stimulations, and results were used to build an inverse model of the neural system. The inverse model was constructed using a kernel adaptive filtering method, and was used to predict the neural stimulation pattern required to recover the pre-lesion neural activity. Applying the derived stimulation to the lesioned network restored the original reaching behavior. This work demonstrates how combining neurocontrol methods with biomimetic brain models can aid the development of neurostimulation protocols that dynamically restore the function of damaged brain regions and the corresponding motor behaviors.

Robert McDougal

Advisor(s): William Lytton
Gordon Shepherd, Michael Hines

Simplifying Model Specification and Interpretation in Computational Neuroscience

The brain makes us who we are as a person, so as a society we have invested much effort into studying how the brain works. This research was originally either animal based or very abstract, but in the 1950s, Alan Lloyd Hodgkin and Andrew Huxley strengthened the basis for computational neuroscience by combining experimental data and the laws of physics to develop a quantitatively predictive mathematical model of an axon, which is part of a neuron, which is the basic computational unit of the brain. Since then, the use of computational techniques to study the brain has grown: the ModelDB repository contains over 950 published computational neuroscience models, and the true total is probably several times higher.

As the use of these models has grown in number and as the models themselves have grown in complexity, it is becoming increasingly important to develop techniques to simplify model construction and to make existing models more understandable so that their quality can be assessed and so that other researchers can build on them safely. To improve model specification, we introduce reaction-diffusion support for the NEURON simulator.

To make existing models more understandable, we present three tools developed for the SenseLab suite of neuroscience databases. ModelView is a web-app for ModelDB that allows graphically exploring the structure (morphology, channel properties, etc) of a computational neuroscience model. ResultView allows exploring the states of a model (membrane potential, current flow, etc) at any time within the simulation. Before these tools, researchers would have had to download, potentially modify, and run the models to obtain this information. Additional insight can come from transforming models out of the virtual world into the physical world; 3-D printing technologies make this possible.

Lindsay Hill

Advisor(s): Youssef Zaim Wadghiri
Jin Kim Montclare, NYU Polytechnic

Neurovascular Changes in Aged C57BL/6 Mice Using Gadolinium Micelle-Enhanced Magnetic Resonance Angiography

Abnormal changes in the neurovascular architecture are associated with numerous conditions including brain tumors, Alzheimer's disease, atherosclerosis, ischemia and diabetes. Mouse models have become invaluable in our understanding, diagnosis and treatment of such conditions, but we have yet to see a longitudinal assessment of neurovascular changes in wild type (WT) control mice. A technique to investigate the vascular architecture of WT mice, including intra-strain variability and changes with age, will serve as a baseline for neurovascular disease models and provide insight into the normal aging process. C57BL/6 was chosen for this study because it is the most widely used strain, but this technique can also be applied to other strains and disease models to monitor vascular changes and therapeutic response. We have employed contrast-enhanced magnetic resonance angiography, a technique used both clinically and pre-clinically, using Gadolinium (Gd)-labeled micelles to achieve in vivo 3D angiograms for monitoring neurovascular changes in C57BL/6 WT mice over two years of aging.

Gd-micelles were synthesized using Gd-DTPA, polyethylene glycol, and rhodamine-bound lipids. Assessment of the micelle size, relaxivity, and plasma half-life confirmed their potential as a long-lived vascular contrast agent. Angiograms of micelle-injected female C57BL/6 WT mice were acquired at ages 2-4 months, 14-16 months, and 24-26 months on a 7-Tesla Bruker micro-MRI system using a 100 μm -isotropic 3D T1-weighted sequence. The resulting brain volumes were aligned and neurovascular changes were assessed quantitatively by intensity-based vascular segmentation.

This technique has enabled longitudinal monitoring of neurovascular changes with high anatomical detail, which we aim to validate using computed tomography and immunohistochemistry. This study serves to increase our understanding of the neurovascular changes that occur with age as well as in diseases of neurovascular involvement.

Alexandra Seidenstein

Advisor(s): William Lytton

Multiscale Computer Modeling of Ischemic Stroke

We are developing multi-scale modeling (MSM) for application in ischemic stroke. The tissue involved in a stroke can be subdivided into a central area of severe ischemia, the ischemic core, and a surrounding area of damaged tissue, the ischemic penumbra. Protection of the penumbra will involve understanding the interactions of multiple cell types and factors: peripheral circulating leukocytes and lymphocytes, microglia, oligodendroglia and astroglial cellular mechanisms, angiogenesis, neurogenesis, synaptic and myelin reorganization, and many intracellular and extracellular signaling processes. Ischemia is typically modeled at two spatial scales: cellular scale (submillimeter) and tissue scale (millimeters to centimeters). The cellular scale focuses on understanding of ionic, neurotransmitter, electrophysiological and ion channel changes in both neurons and glial cells. Tissue level (multicellular) models typically look at the two major regions of interest: 1. The ischemic core, which is the central area whose cells are deprived of oxygen and glucose and will die rapidly, and 2. The penumbra that surrounds the core, where blood flow is low but cells can be saved if blood flow is reintroduced or if cells in this area can be protected. We are augmenting the capabilities of NEURON to accommodate the complexities of modeling in this domain, where electrophysiology interacts with intracellular and extracellular chemical reactions in producing pathophysiology. The new NEURON reaction-diffusion module now provides creation of electrophysiology together with intracellular chemophysiology with potential for extension to the corresponding pathophysiology such as those of ischemia.

Mohamed Sherif

Advisor(s): William Lytton

Multiscale computer model of CA3 of hippocampus for comparing two pharmacological probes of schizophrenia

Schizophrenia (SCZ) involves disturbances at different spatial and temporal scales. Theta (3-7 Hz) and gamma (30-100 Hz) oscillations are abnormal in SCZ. NMDA receptor (NMDAR) antagonists and cannabinoid receptor type 1 (CB1R) agonists are used to model aspects of SCZ. NMDAR antagonism increases gamma and decreases theta power. CB1R agonism decreases both gamma and theta power. We are developing a computer model of CA3 to investigate how the interaction of 3 types of interneurons might explain the difference in oscillatory changes.

Our model consists of pyramidal cells, PV+ basket cells (PV cells), CCK+ basket cells (CCK cells) and Oriens-Lacunosum Moleculare cells (OLM cells). We are currently developing the CCK cells, which are cannabinoid sensitive. These are a regular spiking population of interneurons. They were implemented using calcium-gated potassium channels and voltage gated calcium channels. In comparison to PV cells, CCK cells spiking goes from 40 Hz (in response to injecting 0.2 nA of current) to 70 Hz (in response to 0.45 nA) while PV cells goes from 100 Hz (in response to 0.2 nA) to 170 Hz (in response to 0.45 nA). Implementation of CB1R will be added to the CCK terminals and the recurrent collateral connections between pyramidal cells. To validate the model and the effects of the two pharmacological probes, the frequency bands of the LFP generated by the model will be compared to frequency bands from LFP in rats obtained with and without the drugs by our collaborators.

Multiscale computer modeling is one suitable way to integrate findings from various modalities to reach a mechanistic understanding of the role the different elements play in the etiology and pathophysiology of SCZ. Such an understanding would provide insights into potential treatments which would otherwise be impossible to determine.

Yekaterina Merkulova

Advisor(s): Nicholas Penington
Keith Williams

Intracellular ATP Has Opposite Regulatory Effects on TRPC4 and TRPC5 Channel Activity

TRPC4 and TRPC5 are non-selective cation channels that flux calcium, and therefore their activity may affect many essential cellular processes. TRPC4 channels have been shown to affect signaling in the heart, vasculature, GI tract and the amygdala. TRPC5 affects signaling in the amygdala and the hippocampus. Even though there is high sequence homology and functional similarities between TRPC4 and TRPC5, this lab discovered that intracellular ATP inhibits TRPC5-mediated currents, but potentiates TRPC4-mediated currents. It has been reported that a 1 μ M calcium concentration is necessary and sufficient to activate TRPC5 channels. However, we have found that this is not the case for TRPC4. We hypothesize that the opposing effects of ATP and of intracellular calcium on TRPC4 and TRPC5 currents may be inter-related. Our studies will provide insight into how ATP can affect calcium signaling in normal and pathological states. We are using calcium concentrations of 100 nM (to mimic physiologic levels of calcium) and 1 μ M (to mimic pathological states). Whole-cell and single-channel, voltage-clamp recordings are being performed on HEK293 cells that are transiently transfected with TRPC4, M1 ACh-receptor and eGFP. Preliminary single channel data demonstrate TRPC4 channel activity with a conductance of 33pS, activation by GPCRs and reduced activity at membrane potentials between -20 mV and +20 mV – all characteristics of TRPC4 channels. Intracellular ATP does not affect channel conductance. In whole-cell recordings, a rise in intracellular calcium alone does not induce TRPC4-mediated currents. Future studies will aim to confirm preliminary findings, as well as evaluate the effect of ATP on TRPC4 and TRPC5-mediated currents in the presence of 1 μ M, 100 nM and zero intracellular calcium.

Roza George

Advisor(s): Sheryl Smith

$\alpha 4\beta\delta$ GABAR mediated pruning of dendritic mushroom spines in the prefrontal cortex during adolescence

Dendritic spine density decreases during adolescence in the prefrontal cortex (PFC). Abnormalities in synaptic pruning have been implicated in the development of neurological diseases (van Spronsen and Hoogenrad, 2010) suggesting the importance of this developmental event. Although $\alpha 4\beta\delta$ GABARs are integral in pubertal synaptic pruning in the CA1 hippocampus (Afroz et al., unpublished data), the role that $\alpha 4\beta\delta$ GABARs have in synaptic pruning of other brain regions, or specific spine types, has yet to be examined. By using spine counts, z-stack imaging, and spine classification, synaptic pruning was studied in the PFC to determine the role of $\alpha 4\beta\delta$ GABARs in altering spine density and/or morphology during adolescence. For this study, female C57BL6 wild-type (WT) and $\alpha 4$ GABAR knock out ($\alpha 4$ KO) mice were used soon after puberty onset (~PND 35) or post-pubertally (PND 56). Brains were processed using the Golgi method and spine counts obtained. Data shows that in the WT mice distal dendritic spines are significantly more abundant in the prefrontal cortex during puberty than post pubertally ($t(20)=-3.10624$, $*P<0.05$) which is consistent with pruning (Petanjek et al.,2011). More strikingly, pubertal WT mice have almost three times more mushroom spines on distal dendrites than the post pubertal mice ($t(20)=-3.00096$, $P<0.01$) suggesting that mushroom spines are pruned at puberty. In contrast, the $\alpha 4$ KO post-pubertal mice have significantly more mushroom spines than $\alpha 4$ KO pubertal mice ($t(19)=4.53766$, $*P<0.001$), an amount two-fold greater than WT post-pubertal mice ($t(20)=3.5$, $p<0.001$). These data suggest that $\alpha 4\beta\delta$ GABARs play an important role in the targeted pruning of mushroom spines in the PFC during puberty. Further behavioral studies are needed to understand the possible effects that $\alpha 4\beta\delta$ GABAR mediated reduction of mushroom spines has in the live animal.

Julie Parato

Advisor(s): Sheryl Smith

Kalirin-7 mediates $\alpha 4\beta\delta$ GABAR-induced synaptic pruning in pubertal female mouse CA1 hippocampus

During puberty (PND 35-44, identified by vaginal opening) dendritic spine density decreases by half in the CA1 hippocampus of female mice. This synaptic pruning is due to the increased expression of $\alpha 4\beta\delta$ GABAA receptors (GABARs) at this time. $\alpha 4\beta\delta$ GABARs generate a shunting inhibition, which impairs activation of NMDA receptors (NMDARs) (Shen et al., 2010). NMDA receptor activity has long been associated with LTP and spine maintenance (Kullmann et al., 1992; McKinney, 2010), but the precise mechanism for adolescent spine pruning is as yet unknown.

Kalirin 7 (Kal7) is a rho-guanine nucleotide exchange factor localized to the post-synaptic density. It is necessary for spine stability. Thus, we tested whether Kal7 plays a role in adolescent synaptic pruning. We used immunohistochemical techniques to study Kal7 expression in the hippocampus and Golgi stain to determine spine density changes from z-stack images taken from a Nikon Eclipse Ci microscope. Initially, we showed that the impairment in NMDAR activation at puberty triggers synaptic pruning: Increasing NMDAR expression at puberty with MK-801 (0.1 mg/kg, i.p., 5 d) prevented synaptic pruning, while blocking NMDAR in the post-pubertal $\alpha 4$ $-/-$ mouse produced synaptic pruning. We then tested the hypothesis that NMDARs activate Kal7 expression: In vivo blockade of NMDAR with memantine (10 mg/kg, i.p.) reduced hippocampal Kal7 expression by half ($P < 0.05$), while knock-out of $\alpha 4$ increased Kal7 expression by two-fold ($P < 0.05$), suggesting that NMDAR activation increases Kal7 expression. As predicted, Kal7 $-/-$ have reduced spine density in the CA1 hippocampus during puberty compared to WT mice (spines/ $20 \mu\text{m}$: 16 ± 1.5 , WT, vs. 9.4 ± 0.8 , Kal7 $-/-$, $P < 0.05$). These data suggest that NMDARs increase Kal7 expression, which is necessary for spine stability. Impairment of NMDAR activation via $\alpha 4\beta\delta$ GABARs during puberty reduces Kal7 expression, reducing spine stability, thereby reducing spine density.

Christine Ghobrial

Advisor(s): Mark Stewart

Cardiac Lineage Protein 1 (CLP1) haplodeficiency exacerbates post myocardial infarction injury in mice

Cardiovascular disease is one of the leading causes of death worldwide. Atherosclerosis, for example, can contribute to loss of blood supply to the heart, and damage or destroy cardiomyocytes. A sufficient loss of these cells can lead to heart failure. Cardiomyocyte loss results in a process of remodeling, which includes inflammatory responses that remove debris, followed by fibroblast transdifferentiation to replace muscle tissue.

The Siddiqui laboratory had identified a protein called cardiac lineage protein 1 (CLP1) that is involved in directing cardiac development and made a mouse strain with the gene knocked down. We are exploring whether CLP1 plays a role in remodeling the heart following myocardial infarction in mice. Specifically, we are studying the role of CLP1 in the development of fibrosis in cardiac tissue, and we are studying Smad3 and NF κ B activity, which are known to play a role in myocardial infarction.

Preliminary data show that both wildtype and CLP1 $+/-$ hearts exhibit cardiac remodeling, as measured by percent of collagen deposition, 1 week following ischemic injury both above and below the ligation. CLP $+/-$ hearts had a lower amount of remodeling below the ligation following ischemic injury compared to wildtype.

Also, there is increased pSmad3 and NF κ B activation and translocation into the nucleus in the infarcted zone following ischemic damage in both wildtype and in CLP1 $+/-$ hearts. Cardiac function in CLP1 $+/-$ mice was worse in comparison to the wildtype, as measured by fractional shortening and by ejection fraction. There was not a large difference in LVmass between CLP1 $+/-$ and wildtype mice. Increasing the sample size will better elucidate the impact of CLP1 on the function and remodeling of the heart following ischemic injury.

Data suggest that CLP1 limits the remodeling response by either delaying or by decreasing the amount of collagen deposition in the infarcted area, and result in a poorer functional recovery after ischemic damage.

Tzvi Furer

Advisor(s): Daniel Cukor

Sleep Health in an African American Community Sample

Though racial health disparities across various medical conditions are well documented, sleep health-related disparities are still poorly understood. Sleep pathologies, such as obstructive sleep apnea, are widely associated with various medical complications. Known occupational and personal consequences associated with inferior sleep include decreased productivity and increased risk of physical harm or behavioral accidents. Obstructive sleep apnea is highly prevalent in the general population (1 in 15 adults have moderate to severe OSA) though is disproportionately more prevalent among black populations compared to other groups. Other sleep impairments such as general insomnia and excessive daytime somnolence are also found in greater proportion in black populations. In this study, data collected was part of a screening protocol for a randomized controlled trial of telephone health education intervention for barriers to OSA treatment and assessment. Unique to this study was the involvement of the community in research design, with use of a community based participatory research model to identify conditions and interventions to members of the community. Various community resources were used in promoting recruitment, facilitating participation. In total, 470 people were screened at beauty parlors, churches and health fairs. 72.8% of responders were female, while average age was 41.52 with 42% were born in the United States. The Epworth Sleepiness Index measured excessive daytime somnolence, with 23% of the sample above threshold. Of note, 11% of the sample indicated a moderate to high chance of dozing while driving a car. The sample was divided into 4 discreet pathology groups, including Probable OSA, Insomnia Group, Somnolence Group and No Pathology based on responses to administered questions. Significant group differences emerged, including satisfaction with sleep and self-reported health status, paralleling the continuum of severity of sleep disorders.

Rafik Sidaros

Advisor(s): Stephen Goldfinger

Psychiatric and legal challenges in the care of transgender inmates

Introduction: The definition of Transgenderism varies between the legal and the medical realms.

The percentage of Gender Dysphoria (GD) is much higher among incarcerated individuals than in the general population. This may be a result of societal discrimination or a true higher rate of crime in transgender (TG) individuals. The 8th amendment has long been invoked and intricately tied to access to care for TG inmates. The aim of this study is to compile an overview of policies and laws on TG inmate mental health.

Method: A google scholar search for case law from 1990 to 2015 using the keywords “transgender eighth amendment” yielded 355 cases litigated in the U.S. This was supplemented with a PubMed search for “transgender inmates” and articles focusing on care of inmates with GD were selected.

Results: The TG inmate population faces a unique set of challenges, not the least of which are medical care and housing. The freeze frame policy adopted by many states has been posited to constitute cruel and unusual punishment by some courts. Prohibitive policies expressly denying care for GD have been more readily struck down by the courts as an 8th amendment violation. Violence (including sexual violence) against TG inmates is substantially higher than in the general inmate population. This is directly linked to housing policies of correctional institutions. The financial cost associated with transgenderism complicates the ethical and legal considerations faced by legislators, judges, and prison administrators alike.

Conclusion: The need to involve medical and mental health professionals in housing decisions is gaining recognition by the legislature. The forensic psychiatric community has a great role to play in future research endeavors as well as recommendations for healthcare delivery to these vulnerable and often overlooked patients.

Marla Hidalgo

Advisor(s): Richard McCarthy

Neuroleptic Malignant Syndrome Associated with Clozapine Withdrawal: A Case Report

Abrupt clozapine discontinuation is associated with a psychotic relapse that exceeds in intensity the treatment refractory psychotic symptoms that originally led to clozapine's use. Several other conditions may also occur with clozapine discontinuation including delirium, severe anxiety, altered level of consciousness, somatic complaints, dyskinesia, excited catatonia and neuroleptic malignant syndrome (NMS). Once stabilized, decisions about future treatment must be made. For highly refractory psychotic patients, the loss of clozapine is not trivial. In such cases, patients may never return to their clozapine level of functioning.

This report discusses a patient with treatment resistant schizophrenia who had an ostensible case of clozapine induced NMS in the year before the present hospitalization. Clozapine had been restarted because he had failed multiple medication trials and only responded to clozapine. He again responded well, and was discharged to his home. Months later, he again presented with the abrupt onset of significant signs of extrapyramidal symptoms that rapidly progressed. He had developed an altered mental status, fever, tachycardia, rigidity, and tremor. Urine drug screen was negative. Laboratory tests revealed an elevated CK and transaminases. However, both clozapine and norclozapine levels were undetectable. He was again restabilized. A thorough review of both NMS episodes was undertaken. No risk or precipitating factors were identified other than NMS secondary to covert clozapine discontinuation.

This poster presents how the diagnosis was established, with information about clozapine discontinuation syndromes. The identification of possible clozapine induced NMS is critical as it is a significant risk of non-adherence. In any clozapine patient presenting with an NMS like syndrome, clozapine discontinuation must be a part of the differential. To exclude it may result in patients being denied further clozapine treatment inappropriately.

Anupriya Razdan

Advisor(s): Anupriya Razdan

Clozapine use in HIV + treatment refractory schizophrenia patients: Where does filgrastim fit in?

Introduction: Clozapine is approved for use in treatment resistant schizophrenia. We tried to explore the use of clozapine in HIV positive patients on HAART medication and the possible use of Filgrastim in maintaining the treatment with clozapine in immunocompromised patients.

Method: Review of literature done along with search of hospital database to look for cases of HIV+, treatment resistant schizophrenia on Clozapine.

Discussion: 20-30% of patients are deemed to be treatment refractory and candidates for a clozapine trial. Also, seriously mentally ill patients are 8 times more likely to contract HIV. Hence one would believe that there would be a subset of treatment resistant schizophrenic patients with HIV on clozapine or suitable for clozapine. Search of our database- a state psychiatric facility in a large city, revealed no case of treatment resistant schizophrenia with HIV on clozapine. Review of literature shows very few case reports where HIV positive patients were started and maintained on Clozapine. Additionally, there are few reports but no guidelines about the use of filgrastim in HIV positive clozapine patients, an eventuality that may be necessary in the case of neutropenia, whether or not it was induced by clozapine. Based on the above findings, we studied the possible drug-drug interactions between HAART and clozapine. We have tried to propose some guidelines into the use of clozapine in this population. Our approach is predicated on stratifying patients into different groups based on the presenting WBC/ANC counts, i.e., neutrophil counts. These are, Neutrophil counts within normal limits; Patients with Benign Ethnic Neutropenia (BEN) and those presenting with Neutropenia and the use of Filgrastim in all these groups explained.

Conclusion: We have tried to emphasize the importance of use of Clozapine in treatment refractory HIV + schizophrenia patients and the use of filgrastim to rescue or sustain a clozapine trial in presence of neutropenia.

Arman Fesharaki

Advisor(s): Ramotse Saunders

Moxifloxacin Induced Psychosis: A Case Report Study

Prior studies have demonstrated that the fluoroquinolones can cause drug induced mental status changes (Farrington et al. 1995). These changes, though reported to be less than 0.1%, could potentially manifest themselves as delusional thought process and hallucinations .The reported patient is a 91 year old lady with prior medical history of chronic obstructive pulmonary disease (COPD), hypertension, hypelipidemia , coronary artery disease, peripheral artery disease and no prior psychiatric history. The patient was admitted to the inpatient medical unit for COPD exacerbation, for which she was started on oxygen therapy, prednisone 40mg tab PO daily, monteleukast 10mg tab PO every evening at 7pm, as well as Moxifloxacin 400mg tab PO daily. On the following evening after her admission, the patient became acutely agitated, with paranoid delusions. Despite verbal redirection and reassurance from the staff, the patient remained agitated. The patient also refused all PO medications with continuing psychotic symptoms, Haldol 2.5mg IM was administered. The patient responded favorably to this regimen, and was seen the following day by the consult liaison (CL) psychiatric team. The patient appeared markedly less agitated. Although she remained convinced that the night time staff are still planning to harm her, and she requested immediate discharge. After reviewing patient’s chart, it was verified that this was the first psychotic episode reported per patient. This was the first time that Moxifloxacin was administered for the patient, with no prior exposure to this regimen. In light of prior clinical reports, the CL team recommended discontinuation of this regimen. The patient was reported to be calm the following day, requiring no further psychiatric intervention. Given prior reports of fluoroquinolone induced mental status changes and with rare but possible psychiatric manifestations, due clinical diligence is advised.

Lila Aboueid

Advisor(s): Nitin Toteja

Clozapine-Induced Myocarditis: A Pediatric Case Report

Background: Although known for its efficacy in treatment-resistant schizophrenia, the usage of clozapine has been limited due to concerns over potential adverse effects. Myocarditis, one potential fatal complication, can develop at any point during treatment, but has been most commonly observed 2-3 weeks after initiation.

Objective: A case of acute clozapine-induced myocarditis is described, highlighting the history, onset, and treatment course of presentation. There is a need to raise awareness of this potential complication, especially in the pediatric population.

Results: 17-year-old Puerto Rican boy, with history of schizophrenia, disorganized type (treatment resistant) and intellectual disability, developed myocarditis on the thirteenth day following clozapine commencement. Initial presenting symptoms included tachycardia, lethargy, and vague gastrointestinal distress. Patient fully recovered after supportive medical care, clozapine discontinuation, and medication adjustments.

Conclusions: Myocarditis is a known potential complication of clozapine initiation, however due to its limited usage in the pediatric population, reported cases are limited. There is a need to establish evidence based monitoring guidelines for clozapine usage, as the presentation may be atypical and clinical suspicion may be overlooked.

Jyothsna Karlapalem

Advisor(s): Susan Whitley

“Real Play” based curriculum is effective in motivating students to learn Motivational Interviewing

Background: Motivational Interviewing (MI) is an evidence based tool to change target behavior. As time available is the most common limiting factor in MI training, we developed a brief (1.5hr), single session curriculum involving “real play” (talking about a chosen area of change in one’s own life), with the aim of motivating students to learn MI in their own time.

Objectives: To demonstrate the efficacy of real play based curriculum to motivate students to learn MI in their own time and to validate the ability of this method to increase perceived importance of learning MI, belief in MI as an effective tool to bring about behavior change.

Methods: Our curriculum was piloted on volunteers from first year medical students.

Format: Pretest, brief introduction - 15min, Real play with student counselor- 15min, (One student “real played” as client, with self-chosen specific health related target behavior and another student played the counselor), Power point presentation on MI- 20min

Real play with instructor counseling using brief MI approach- 15min, Wrap up and Q &A- 15min, Post test- 10min. Pre and post- test questionnaires were paired, included importance, readiness and confidence rulers, Likert scaled questions and space for subjective feedback, and did not contain identifying data. Results were analyzed using two tailed paired t tests.

Results: Students reported significantly increased belief in effectiveness of MI and increased importance of learning MI after the session. Ten out of eleven students expressed willingness to attend next session to learn MI. All students reported that the interactive parts of the session were more useful, and wanted more time allotted for that.

Conclusions: Results indicate that our curriculum is effective in motivating students to learn MI. This model might be applicable in teaching MI across a range of clinicians including case managers, social workers, nurses and physicians.

Furqan Nusair

Advisor(s):

The Right To Keep And Bear Arms When Mentally Ill

The right to keep and bear arms as it applies to persons with mental illness is not often addressed in the US. Mass shooting continue to result in unheeded calls for Congress to enact federal gun control legislation with some states, namely Connecticut and New York, choosing to enact their own legislation. New York’s SAFE Act of 2013, touted as the ‘toughest gun control law’ in the US to date, mandated the reporting of persons that are likely to engage in conduct that would result in serious harm to self or others by mental health professionals with provisions for loss of firearms. Although broad and overly inclusive, information is lacking to evidence whether it has been effective in keeping firearms out of the hands of dangerous persons or whether it has reduced violent crime.

Current federal legislative standards prohibiting mentally ill persons from acquiring firearms are examined and the effect of the SAFE Act on mental health providers, patients and crime rates in New York is investigated. Firearm loss and violent crime post SAFE Act are discussed. Further research evaluating US gun control policies is made with a comparison drawn to the Australian experience following the Port Arthur shooting.

Subhash Chandra

Advisor(s): Carole Chaski
Jeffrey Wilkinson

Computational Analysis Of Hindi Suicide Notes Reflects Universality of Suicide Themes

Introduction: Suicide notes play a pivotal role in death investigation. Pestian (2013) reports 50% accuracy for mental health professionals differentiating real from simulated suicide notes. SNARE (Suicide Note Assessment REsearch) software classifies texts as a suicide note or control text-type with accuracies from 80%-88%, depending on text length, on a database of ~1,000 English texts.

Objective: Can SNARE work cross-culturally to provide support for identifying notes?

Method: 15 suicide notes were collected from 33 cases of suicide confirmed by autopsy findings, psychological autopsy, inquest paper, and crime scene investigation. 13 legible notes were translated into English by the first author (a native Hindi, fluent English speaker). The translated notes were run through SNARE.

Results: SNARE classified 8 of 13 translated texts as suicide notes (61.5%) and 5 as control texts (38.5%). All the mis-classified notes were longer than 80 words.

Conclusion: With limitation of translation, and lower accuracy of SNARE at high word count, accuracy of 61.5% is higher than that of humans in differentiating between true and simulated suicide notes. Supplemental research includes (i) using a different translator with a literary rather than scientific background and re-testing the data on SNARE, and (ii) creating a Hindi version of SNARE.

Nicole McLean

Advisor(s): Michael Joseph

Promoting Health Advocacy and Policy Change Among Students of Color: The Health Disparities Summer Internship Program

Background: Communicating the benefits of effective health policy is emphasized through an exciting summer internship program for high school students of color. The Health Disparities Summer Internship Program (HDSIP) of the Brooklyn Health Disparities Center introduces students to a curriculum consisting of: awareness of health disparities, basic research skills, and community-based participatory research methods. We describe the results of a survey that assessed the program's impact on its participants.

Methodology: A total of 57 students participated in the 4-week HDSIP within the years 2012, 2013 and 2014. Students attended lectures covering topics such as health disparities, health in America, immigrant health, and policy and advocacy. While working with community-based organizations, students gained hands-on experience related to issues discussed in class. Students completed and presented research projects and provided suggestions for health policy change. Pre/post surveys were completed to assess the impact of the program.

Results: At the beginning of the program, 75% of students reported being interested in incorporating advocacy into their future careers; by the end of the program the percentage rose to 94%. After familiarizing students with CBPR and health advocacy, 81% of students planned to advocate for changes in their community; an increase from the initial 63%.

Conclusion: Increasing diversity in the health workforce has widely been proposed as a means of addressing health disparities. Introducing minority students to health professions can serve as a catalyst for lasting changes in health outcomes. The HDSIP has increased students' awareness of social determinants of health and has fostered their interest in improving the health of minority populations.

Shaunte Truick

Advisor(s): Michael Joseph

Advancing Primary Care Systems to Eliminate Health Iniquities

Background: According to the Institute of Medicine Report written by the National Academy of Sciences, “The number of patients visiting Emergency Departments has been growing rapidly. Emergency Rooms (ERs) across the country are overcrowded.” (Warden, 2006)

Objective: Individuals should be informed about Urgent Care (UCC) and Community Health Centers (CHC). This will ultimately reduce overcrowding in ERs, allowing people to utilize these facilities.

Method: A minimal six-item survey assessed the participants’ awareness to CHCs and their usage of local UCCs. The surveys were administered to 100 people, 25 surveys to each of four major hospitals in low-income and high-income areas. The recruitment sites were Kings County Hospital, University Hospital of Brooklyn (“low-income”), and Methodist Hospital, Brooklyn Hospital Center (“high-income”). Adults of various race/ethnicities participated in the surveys. Brownsville Family Health Center, and Bedford Stuyvesant Health Center were also contacted and inquired about their policies on urgent care. An additional informal interview was conducted with a representative of CITY MD evaluating the reasons for the lack of UCCs in low-income neighborhoods.

Results: The results showed that 71% of individuals have primary care providers leading them to not use the CHC’s as well as not being aware of the location. Only 6% of individuals surveyed use UCCs, while 65% of individuals prefer to go to the ER. There was no significant difference in the level of awareness of the facilities in low or high-income areas.

Conclusion: Although UCCs provides services for a wide variety of injuries, the lack of awareness constitutes for a major reason the ER is preferred, which leads to overcrowding in the ER. These results can further assist the American Cancer Society in developing new strategic health initiatives that support their mission to increase the usage of CHCs and UCCs.

Allison Sih

Advisor(s): Dawn Kopp

Effect of parity on the epidemiologic profile of Malawian women presenting for obstetric fistula repair: a cross sectional study

Introduction: The population of women who are multiparous at the time of obstetric fistula formation has rarely been described. Our objective is to describe the patient population presenting for obstetric fistula repair at Bwaila Maternity Hospital in Lilongwe, Malawi and to identify potential risk factors that may contribute to fistula formation, particularly among multiparous women.

Methods: We completed a cross-sectional analysis of baseline data from women who presented for obstetric fistula repair between September 2011 and July 2014. A survey of their demographics, obstetric history, physical exam findings, and operative notes were collected. Women with fistula from non-obstetric causes were excluded. Chi-square, Fischer exact, and Mann-Whitney tests were used. IRB approval was obtained from the Malawi National Health Sciences Research Committee and the University of North Carolina IRB.

Results: Of the 459 women who presented to Bwaila Hospital, 195 patients (42.5%) were primiparous and 258 (56.2%) were multiparous at the time of fistula formation. The median parity for multiparous patients at the time of fistula formation was 3 (IQR 2-4). Multiparous patients were more likely to have a liveborn infant at that delivery (29.7% vs 15.9%, $p=0.001$), to labor less than 24 hours (55.8% vs 40.0%, $p=0.001$), and to have a Caesarean delivery rather than a vaginal delivery (58.7% vs 49.0%, $p=0.041$). There were no significant differences in occupation, education level, or age at first marriage.

Discussion: Unlike previous studies, the majority of patients presenting for repair at Bwaila Hospital were multiparous at the time their fistula formed. This study highlights the population of women with obstetric fistula is diverse and even older and multiparous women are at-risk for developing fistula. Further understanding the factors that lead to obstetric fistula in multiparous patients is key to eliminating this condition in low-income countries.

Andrew Abdelmalek

Advisor(s): David Seligsohn

Post-operative hyponatremia with altered mental status

39 year old female who presented for bilateral inferior turbinaculectomy. PMH of HTN controlled with nifedipine, BMI of 33.3, OSA without CPAP, and migraine headaches treated with topiramate. She was compliant with home medications. Pre op VSS, unremarkable physical exam, and airway. Labs were WNL.

Operation was uneventful. At emergence, patient's blood pressure rose to 180/110. When she met extubation criteria, she was extubated, following commands and protecting her airway, and transported to the PACU. In PACU her blood pressure was still elevated with SBP in the 170s, but was mentating well and otherwise stable. After 4 hours she had a heart rate of 82 and blood pressure of 152/91, was meeting discharge criteria, and about to be sent home when she became tachycardic to low 100s and hypertensive to 170s a/w complaint of pressure in her head. Her BP was aggressively treated including taking her home meds. An hour later, she was still complaining of pressure in her head. and her mentation began to deteriorate. She was pausing between sentences and starting to have muscle flaccidity. Considering hypertensive emergency, an arterial line was placed, a nitroglycerin drip started, and her systolic pressure came down to the 140s with titration. her pressure around head was improving but she now paused midsentence when speaking, and her pupils were dilated but responsive. Neurology was consulted, STAT head CT showed blunting of the sulci between the cerebellum and cerebrum, indicating early cerebral edema. Pt had no focal deficits but showed weakness throughout, had dilated but responsive pupils, and was obtunded. STAT CBC and CMP revealed the only abnormality being a sodium of 129. Serum osmolarity was WNL. MICU was consulted, the patient was accepted and started on 3% NS at 35 ml/hr. The next morning, her mental status had improved and serum sodium rose to 132. SIADH was diagnosed. Patient continued to improve clinically in ICU and was discharged home from ICU.

Shama Patel

Advisor(s):
Furqan Nusair

Human trafficking: federal legislation enabling prevention, protection, prosecution with ongoing challenges

The Victims of Trafficking and Violence Protection Act of 2000 aimed to combat trafficking in persons, a contemporary manifestation of slavery whose victims are predominately women and children, to ensure just and effective punishment of traffickers, and to protect their victims. Human trafficking is estimated to value \$31.6 billion per annum. An ongoing increase in human trafficking continues with the majority involving sex trafficking, labor trafficking or a combination of both.

An examination of the current federal legislative framework in preventing human trafficking, protecting victims, and prosecuting human traffickers is undertaken with identification of currently available supports for identified victims. Challenges in screening, identifying and supporting victims of trafficking are discussed, including the lack of validated tools for use in the forensic mental health service setting. Resources are identified to assist the victims of trafficking and their service providers.

Andrew Aherne

Advisor(s): Richard Sinert

Emergency Department Central Line Confirmation with Saline Flush and Bedside Echocardiography: A Prospective Study

Post-procedural chest X-ray is standard of care to confirm correct position after placing a central venous catheter (CVC). This prospective observational study tests the difference in confirmation times by bedside echocardiography bubble test as compared to x-ray.

After CVC placement, confirmatory x-ray was ordered. Simultaneously, a bubble test was performed by injecting agitated saline through the CVC while a bedside echo was performed (Subxyphoid, parasternal long, or apical four view). The appearance of the saline, in the form of opacification of the right atrium and ventricle, signified appropriate placement. Time from line placement to this confirmation was then compared to the time from CVC placement to x-ray confirmation. Times (X-ray vs. Echo) were presented in Minutes as medians with intraquartile (25%,75%) ranges. Confirmation times were compared by Mann-Whitney U.

Results: We enrolled 53 subjects (Subclavian [n=2] and Internal Jugular [n=51]) age range 26-93 years, in the ER (n=42) and ICU (n=11). Indications for CVC were shock and inability to obtain peripheral access. Operators were emergency residents (n=38), ultrasound fellows (n=2), or ultrasound faculty (n=1). The bubble test successfully confirmed 100% of the central lines placed, and was performed prior to the availability of x-ray confirmation in 95% of cases (51/53). The median time to confirmation by ultrasound of 20 minutes (IRQ 13, 26) was significantly ($p<0.001$) shorter, than the 38 (IRQ 28,53) minutes by x-ray. In the ED, median time to confirmation by ultrasound was 20.5 minutes (IRQ 15, 27.75), compared to median time to x-ray of 39.5 minutes (IRQ 30.75, 60.25). In the ICU, median time to confirmation by ultrasound was 16 minutes (IRQ 11, 20), compared to a median time of 35 minutes (IRQ 20, 65) by x-ray.

The ultrasound-assisted bubble test is a safe and rapid means of confirming CVC placement, and allows for rapid use of the line compared to x-ray in both the ED and ICU setting.

Jennifer Chao

Advisor(s): Richard Sinert

Predictors of an Abnormal Chest X-Ray in Emergency Department Patients Suspected of Bronchiolitis: A Systematic Review

Background: Despite national guidelines, that state “current evidence does not support routine radiography in children with bronchiolitis”; use of CXR in these patients is high. Excessive use of CXR not only exposes children to excess radiation, but increases the cost of care. An evidence-based approach defining the utility of CXR in bronchiolitis would aid practitioners when deciding whether or not to image a particular patient.

Objectives: We performed a systematic review to describe potential predictors of a CXR inconsistent with simple bronchiolitis.

Methods: We searched the medical literature from 1965 to 11/2014 in Pubmed / EMBASE using a strategy by a medical librarian from the following PICO formulation of our clinical question: Patients: Pediatric Emergency Department patients (< 2 years) suspected of Bronchiolitis. Intervention: Age, History, Physical Exam and Vital Signs. Comparator: Abnormal CXR defined as atelectasis vs infiltrate or other finding inconsistent with bronchiolitis. Outcome: Operating characteristics of H&P and VS predicting an abnormal CXR were calculated: Sensitivity, Specificity, and Likelihood Ratios. The methodological quality of the studies was assessed using the quality assessment of studies of diagnostic accuracy tool (QUADAS-2). Data analysis was performed using Meta-DiSc with a random-effects model.

Results: We found 5 studies including 1,129 patients meeting inclusion/exclusion criteria. Prevalence of an abnormal CXR ranged from 7%-23%. Significant heterogeneity within each predictor was too large for data pooling. Although 4/5 studies were prospective, 3 only included first episodes of wheezing. In 3 studies every patient in the study received a CXR where as in 2 the CXR was obtained at physician discretion. Furthermore, not every study presented each clinical predictor.

Conclusion: No single predictor of an abnormal CXR was of sufficient strength to initiate or preclude ordering a CXR in a child with clinical bronchiolitis.

Ashika Jain

Advisor(s): Richard Sinert

History, Physical Exam plus Laboratory Testing and Ultrasonography for the Diagnosis of Cholecystitis: An Evidence-Based Review

Background: Acute Cholecystitis (AC) is a common differential for patients presenting to the Emergency Department (ED) with abdominal pain. Objectives: Systematic review of History/Physical exam (H&P), Laboratory studies and Ultrasonography(US) in diagnosing AC in the ED.

Methods: PUBMED and EMBASE search from 1965 to 11/2013 using PICO formula: All patients in ED suspected of AC; H&P, laboratory studies and US findings commonly used to diagnose AC; Surgical pathology confirming AC; Operating characteristics of interventions in diagnosing AC were calculated: Sensitivity, Specificity and Likelihood Ratio of Positive (LR+) and Negative Test (LR-). Studies assessed via Quality Assessment Tool for Diagnostic Accuracy Studies. Data analysis performed using Meta-DiSc with random-effects model (95% CI)

Results: Separate Pubmed / Embase searches retrieved studies for: H&P (n=732), Labs (n=74) and US (n= 474). 8 H&P studies met inclusion/exclusion criteria with prevalence 9%-64%. Fever (>101F) Sens. 36% (26%-46%), and Spec. 80% (71%-86). LR+1.73 (0.83-3.58), LR- 0.81 (0.58-1.12). Jaundice Sens. 11% (7%-16%), and Spec. 99% (98%-99%). Pooled LR+ 3.38 (0.34-34.01), LR- 0.95 (0.95-0.85). Murphy's sign Sens. 62% (56%-68%), Specif. 94% (93%-98%). LR+ 6.53 (0.194-21.94), LR- 0.46 (0.32-0.67). Right upper quadrant pain Sens. 56% (50%-62%) and Spec. 70% (68%-72%). LR +3.35 (0.73-15.27), LR- 1.13 (0.16-7.88). Lab studies (n= 3) with prevalence 5%-26 %. Elevated Sens. 40% (12%-74%), and Spec. 93% (77%-99%). LR+ 5.80 (1.25-26.99), LR- 0.64 (0.39-1.08). 4 US studies, prevalence 10%-37%. Sens. US 88% (78%-94%) Spec. 71% (65%-76%). LR+ 3.23 (1.74-5.99), LR- 0.18 (0.10-0.33).

Conclusion: Variable disease prevalence coupled with decreased sample size, increases risk of selection bias. Individually, these parameters cannot reliably rule-out AC. Development of a clinical decision rule to include H&P, laboratory data and ultrasound are more likely to achieve correct diagnosis of AC.

Jennifer Martindale

Advisor(s): Richard Sinert

Calcium Channel Blockers versus Beta-Blockers for Acute Rate Control of Atrial Fibrillation with Rapid Ventricular Response: A Systematic Review

Background: Rate control is the preferred therapeutic intervention in stable patients with rapid ventricular response to atrial fibrillation when the onset of atrial fibrillation is unknown. Clinical guidelines recommend either calcium channel blockers or beta-blockers as rate control agents.

Objectives: This is a systematic review of the literature to compare the efficacy of calcium channel blockers with beta-blockers for rate control of atrial fibrillation with rapid ventricular response

Methods: We searched PubMed, EMBASE, and the Cochrane Registry for trials from 1965 through 11/2013 using a search strategy aimed to compare the relative efficacy of beta-blockers and calcium channel blockers for reduction in ventricular rate. Relative risk was calculated using Review Manager (RevMan). Methodological quality of included studies was evaluated.

Results: Our search yielded 1003 unique studies. Seven studies met our inclusion criteria. Four were available only in abstract format and 2 provided insufficient data. This left a single double blind, randomized study of 40 patients comparing IV diltiazem (0.35 mg/kg) with IV metoprolol (0.15 mg/kg). Successful rate control was defined as a reduction in heart rate by 20% or a heart rate less than 100 bpm. Diltiazem and metoprolol were successful in achieving rate control in 65% and 50% of patients, respectively. Relative risk of rate control by diltiazem versus metoprolol was 1.13 (95% CI 0.86-1.46). None of the patients in either group experienced hypotension or bradycardia. Lack of a predetermined sample size was a major methodological concern that challenged this study's internal validity.

Conclusion: The evidence to support one drug over another for the treatment of AF with rapid ventricular response is extremely limited. Randomized trials with larger and predetermined sample sizes are needed to establish which agent is more effective.

Adam Aluisio

Advisor(s): Shahriar Zehtabchi

Correlation of venous lactate and time of death in emergency department patients with non-critical lactate levels and mortality from trauma

Serum venous lactate levels (LAC) help guide emergency department (ED) resuscitation of patients with major trauma. Critical LAC level (CLAC, ≥ 4.0 mmol/L) is associated with increased disease severity and higher mortality in injured patients. The characteristics of injured patients with non-critical LAC (< 4.0 mmol/L) (NCLAC) and death has not been previously described.

Objectives: 1. To describe the characteristics of patients with venous NCLAC and death from trauma. 2. To assess the correlation of venous NCLAC with time of death.

A Retrospective cohort study at an urban teaching hospital between was undertaken between 9/2011 and 8/2014. Patients were included if they met all criteria: 1. Admitted through the ED, 2. LAC drawn at time of initial ED evaluation, and 3. Died during the index hospitalization. Exclusion: CLAC. Outcome: Correlation of NCLAC and time of death. Data were extracted from an electronic medical record by trained data abstractors using a standardized protocol. Cross checks were performed on 10% of data entries and inter-observer agreement was calculated. Data were explored using descriptive statistics and Kaplan-Meier curves were created to define survival estimates. Data are presented as percentages with 95% CI for proportions and medians with quartiles for continuous variables. Kaplan-Meier curves with differences in time to events based on LAC are used to analyze the data.

60 patients met the inclusion criteria. The median age was 51 years (quartiles: 30,75) and 73% were male, age range 2 to 92). The median LAC in the overall cohort was 1.9 mmol/L (quartiles: 1.5, 2.1). Twelve patients (20%) died during the first 24 hours with two (17%) due to intracranial hemorrhage. The median survival time based was 13 days (95%CI: 5-19 days) (Figure). The clinical characteristics of the entire cohort will be reported.

In trauma patients with NCLAC who die during the index hospitalization, the median survival time is 13 days.

James Willis

Advisor(s): Shahriar Zehtabchi

Testing the utility of a novel education model for training emergency medicine residents in delivery of death notification

Death Notification (DN) is a critical topic in emergency medicine (EM) that lacks standardized training protocols. The objectives of the study are to compare methods in teaching DN to residents and to validate a DN scoring system (SPIKES) in the emergency setting.

This is a pilot randomized controlled trial enrolling EM residents from two urban institutions. Residents were randomly assigned to one of the three groups: small group training session, a didactic lecture on DN and a lecture unrelated to DN (control). Primary outcomes: performance in each study group during a high fidelity simulated DN scenario using SPIKES score provided by board certified PC faculty blinded to the group assignments. The DN scenario was conducted after an ACLS simulation case. Secondary outcome: inter-evaluator consistency for SPIKES scores provided by the faculty evaluating each resident.

Thirty-seven residents were enrolled and assigned to 3 study groups (12 control, 12 lecture, and 13 small group). Mean scores differed significantly for small group vs. control ($p=0.002$) but not for control vs. lecture ($p=0.053$). Lecture did not differ significantly vs. small group ($p=0.589$). Results were similar for the analysis controlling for PGY status. Inter-evaluator ICC was estimated at 0.70 across all assessors.

This high fidelity simulation-based evaluation model designed for DN showed better performance by residents assigned to small group sessions unlike other literature on this topic where no specific intervention was superior. This method of objectively testing educational interventions can be used to incorporate important aspects of PC as well as other topics into EM curriculum. Unlike most educational literature using subjective surveys this methodology produces quantifiable evidence of the effectiveness of an intervention. SPIKES is an appropriate tool for evaluating residents' DN training. It has been used in other trials but the inter-rater reliability never published.