

Andrea Birnbaum

Advisor(s):Madhavi Gavani, Eve S Faber, Andrea Birnbaum, and Richard Sadovsky

**Who Really Manages Patients' Medications? A study of inner city adults over 40 years of age.**

Objectives: / To determine if our patients are being assisted by another individual in managing a significant phase of medication management and identify and predict the patients being assisted, using clinical characteristics such as number of chronic diseases or number of medications. / Methods: / A survey was utilized to determine how patients manage their medications and when they are assisted by another individual. A trained surveyor verbally administered the survey to consenting adults > 40 years of age coming to an inner city primary care center. The responses were quantitatively analyzed. / Results: / 61 patients (43% of total surveyed) receive assistance with medication management. Majority reported getting assistance from a family member; 28 (46.6%) reported this assistance during phase 1, 11 (18.6%) reported this during phase 2, and 17 (28.8%) reported this assistance for phase 3. The only other person identified more than rarely was the pharmacist, with 22(36.7%) patients reporting that the pharmacist helped them with phase 1. There was a statistically significant trend showing a direct relationship between both the number of chronic diseases and the number of medications with the need for assistance with one or more phase of medication management. Some of the limitations were that only a small number of patients were surveyed and the clinical information was unavailable for some. / Conclusion: / Many patients are receiving help with one or more phases of medication management. Family members are the major source of medication assistance for our patients. Family members who are helping patients with medication management need to be educated about medication use and informed about medication changes. The care team needs to reach out to helping family members and encourage them to accompany patients to their clinic visits. Patients with higher numbers of chronic diseases and/or are using more medications are more likely to receive help from others. /

Frank S Cautela

Advisor(s):Carl B Paulino

**Spine Injuries in Child Abuse**

Background: Although rare, spinal injuries associated with abuse have devastating implications in the pediatric population. We analyzed the association of pediatric spine injury in abused children and determined the anatomical level of the spine affected, while also focusing on patient demographics, length-of-stay, and total hospital charges compared to non-abused spine patients. / Methods: A retrospective review of the Kids' Inpatient Database was conducted from 2000-2012 to identify pediatric patients (<18 years) who suffered vertebral column fractures or spinal cord injuries. Patients with a documented diagnosis of abuse were identified using ICD-9-CM diagnosis codes. Our statistical models consisted of multivariate linear regressions that were adjusted for age, race, and gender. / Findings: There were 22,192 pediatric patients with a diagnosis of spinal cord or vertebral column injury during the study period, 116 (0.5%) of which had a documented diagnosis of abuse. The most common type of abuse was physical (75.9%). Compared with non-abused patients, abused patients were more likely to be less than 2 years of age (OR=133.4), female (OR=1.67), and non-white (Black: OR=3.86; Hispanic OR=2.86; Other: OR=2.33). Abused patients also presented with an increased risk of thoracic (OR=2.57) and lumbar (OR=1.67) vertebral column fractures and had a multivariate-adjusted mean length-of-stay that was 62.2% longer ( $p<0.001$ ) and mean total charges that were 52.9% higher ( $p<0.001$ ) compared to non-abused patients. / Discussion: Spine injuries are rare but can be found in the pediatric population. With an additional documented diagnosis of abuse, these injuries affect younger patients in the thoracolumbar region of the spine, and lead to longer lengths of stay and higher hospital costs when compared to non-abused patients. Physicians should maintain a higher level of suspicion of abuse in patients with spine injuries. /

Thomas Duggan

Advisor(s): Kay Beharry and Jacob Aranda

**Effects of High and Low Doses of Caffeine Citrate on Biomarkers of Angiogenesis in the Neonatal Rat Lungs Exposed to Hyperoxia and Intermittent Hypoxia**

Background: Caffeine Citrate, a methylxanthine that is commonly used across the world, has been proven to play a significant role in decreasing various neonatal morbidities and mortality, however there is continued debate over the appropriate dosing. Extremely low gestational age neonates often experience brief episodes of hypoxia, or intermittent hypoxia (IH) during oxygen therapy and are routinely treated with Caffeine. Currently, there are no studies regarding the effects of high versus low dose Caffeine on the development of angiogenesis in the preterm lung exposed to IH. / Objective: Test the hypothesis that caffeine (C) at different pharmacologic doses augments lung biomarkers of angiogenesis in IH with hyperoxia. / Materials/Methods: Rat pups were randomized to room air, 50% O<sub>2</sub> or IH + hyperoxia - consisting of hyperoxia (50% O<sub>2</sub>) with brief episodes of hypoxia (12% O<sub>2</sub>). Each group was treated with either: 1) Hi-C: loading dose (80 mg/kg) day 0; maintenance dose (20 mg/kg) days 1-14; 2) Lo-C: loading dose (20 mg/kg) day 0; maintenance dose (5 mg/kg) days 1-14; or 3) equivalent volume saline on days 0-14. Biomarkers of angiogenesis (HIF1 $\alpha$ , VEGF, sVEGFR-1, VEGFR-3 and IGF-1) were determined in the lungs. / Results: Lung VEGF and IGF-1 were preserved with low dose caffeine compared to high dose caffeine with IH. HIF1 $\alpha$  and VEGFR-3 levels were found to be decreased in the Low-C groups exposed to IH. Groups exposed to 50% hyperoxia had increased levels of VEGFR-3 with Low-C and saline compared to Hi-C dosing. / Conclusions: Low dose caffeine preserved VEGF and IGF-1 levels compared to high dose caffeine. Elevated HIF1 $\alpha$  levels and decreased VEGF in IH with high dose caffeine demonstrated poor pulmonary vascular development. Caffeine Citrate appears to alter lung biomarkers of angiogenesis in a dose dependent manner. This balance in dosing may be a crucial point for the preservation of normal pulmonary vascular development in neonates routinely being treated with caffeine.

Lindsay Hill

Advisor(s): Jin Montclare and Youssef Zaim Wadghiri

**Protein-Engineered Ferrofluid for Theranostic Applications**

Magnetic therapeutic delivery systems have increasingly been exploited in biomedical applications including magnetically-driven drug delivery, therapeutic hyperthermia, and diagnostics, serving as magnetic resonance imaging (MRI) contrast agents. Ferrofluids, liquids comprised of iron-based nanoparticles, are of particular interest because iron oxide (FeOx) is functionalizable and well tolerated in vivo. Here, we aim to develop a protein-based ferrofluid for chemotherapeutic delivery. / Our system is based on a variant of the coiled-coil domain of the Cartilage Oligomeric Matrix Protein, maintaining a hydrophobic pore for binding small molecules, such as anti-neoplastic curcumin, which fluoresces once bound within the pore. The variant, Q, has been engineered to maintain charged surface patches for assembly into nanofibers and, upon curcumin binding, mesofibers. We employ residue-specific incorporation to synthesize an azide-functionalized Q capable of azide-alkyne cycloaddition to an alkyne-functionalized peptide CMms6, which templates and organizes FeOx crystallization. Subsequent FeOx nanoparticle synthesis in the presence of Q-CMms6 forms a ferrofluid of magnetically-functionalized drug-carrying fibers. / / Transmission electron microscopy (TEM) and fluorescence microscopy are used to characterize fibers from the nanoscale (~600nm diameter), to mesoscale, (~35 $\mu$ m diameter). Nanoparticle features are assessed with TEM, revealing cuboidal FeOx particles 7nm in diameter. Ferrofluid magnetic susceptibility is confirmed with magnetic manipulation and MRI darkening potential is quantified at 7-Tesla. MRI confirms a 3-3.4-fold darkening effect compared to a buffer control, showing promise for imaging. / / By taking advantage of a biologically synthesized drug-carrying protein and bioinspired templation of FeOx, this ferrofluid may serve as a biocompatible drug-delivery vehicle. Its therapeutic properties and diagnostic potential for MRI yield a novel theranostic agent.

Amir Momeni Boroujeni

Advisor(s):Raavi Gupta

**Application of cell-graphs and multilayer perceptron for computerized diagnosis of breast lesions**

Robust placental functioning is essential to the survival of developing fetuses. We hypothesize that placental lesions in fetal autopsies follow a number of patterns. / Design: Autopsy and placental reports of all cases of intrauterine fetal demise at SUNY Downstate Medical Center during 2013 - 2014 were retrospectively reviewed. A network was constructed from the placental findings with each node representing a placental observation. The edges represent weighted associations between these observations. We explored the network characteristics of placental lesions. / Results: 58 cases of intrauterine fetal demise with a mean gestational age of 22.83 (14-39) were included in this study. We identified 20 significant placental lesions and 286 associations with 69 significant associations ( $p$  value  $< 0.01$ ). The mean degree was 15.053. The mean power was 0.863. Dysmorphic villi, hypoplastic tertiary villi, hydropic villi, x-cell hyperplasia, trophoblastic buds, trophoblastic inclusion cysts and fetal vasculopathy had the highest power in the network. Cluster analysis showed clusters of highly associated placental pathologic findings. By application of gestational age for layer definition two clusters of highly associated placental lesions were identified: in the second trimester the cluster included dysmorphic villi, hydropic avascular villi, trophoblast inclusion cysts, X-cell hyperplasia and hypoplastic tertiary villi. In the third trimester the cluster included fetal vasculopathy, hypoplastic tertiary villi, chorangiomas, chorangiomas, increased trophoblastic buds, intervillous hemorrhage, chorioamnionitis and funisitis. / Conclusion: Network analysis is a novel method of looking at data. It is especially useful in identifying patterns and clusters. Using this approach we have shown that placental lesions associated with intrauterine fetal demise follow an identifiable pattern.

Marguerite Orsi-Canter

Advisor(s):Madu Rao

**Changes in pediatric residents' perceptions of task/role comfort level during patient code scenarios; results of a simulation mock code training program**

Background: In modern pediatric medicine, trainees are less frequently exposed to emergent code situations. PALS recertification is conducted every two years, potentially giving residents minimal exposure between certification and actual codes. This gap poses a risk for a decrease in skills but also engenders a lack of confidence. Simulation mock codes can be used in training programs in an attempt to maintain skills and comfort. However, there is no data analyzing resident comfort level with specific tasks and roles in a code situation. / Objective: Examine resident comfort levels regarding code roles and tasks and how they change with repeated high frequency, high fidelity, in-situ mock code simulations with Video Documented-Debriefing (VDD) during their inpatient rotations. / Methods: We conducted a prospective, observational study by implementing sporadic mock codes on each PICU and inpatient units at SUNY Downstate and Kings County Hospital Center. After the mock codes, anonymous surveys were administered to residents to document their perceptions of comfort and competence in 9 different roles within a code scenario. / Results: 58 post test datasets were collected and plotted against the number of codes. Resident's confidence performing chest compressions significantly trended up by mock code number 6; there was a slight improvement assuming the role of code leader. Confidence in communication all decreased by code number 6. The remainder of the roles remained relatively unchanged. / Conclusions: Resident's increased confidence in their compression and leadership skills are likely attributed to repeated codes incorporating VDD on a mannequin capable of giving chest-compression feedback. Resident's decreased sense of comfort in communication is likely due to an initially falsely-elevated, preconceived notion of ability to communicate during codes.

Michael Sangobowale

Advisor(s):Peter Bergold

**MINO plus NAC synergistically treats TBI within a clinically relevant therapeutic window.**

Currently there are no effective treatments for TBI. We have previously shown that the combination of FDA-approved drugs minocycline (MINO) and N-acetylcysteine when dosed 1-hour after injury synergistically improves both cognition and memory, modulates inflammation, limits grey matter injury and induces remyelination. The dosing window of MINO plus NAC needs to be explored to determine its utility as a therapeutic. In a rat controlled cortical impact model (CCI) of TBI. We report that MINO and MINO plus NAC improved cognition and memory when dosed 24-hours after injury. This therapeutic window was assessed using two behavioral tasks. In the active place avoidance task, a task with high cognitive demand. MINO plus NAC, improved cognition in the rat CCI model when dosed 12-hours after injury. The 12-hour therapeutic window of MINO plus NAC was increased to 24-hours using Barnes maze, a behavioral task that likely has a lower cognitive demand than active place avoidance. When dosed at 1-hour MINO plus NAC increased myelin content in white matter regions that lost axons, supporting the hypothesis that the drug combination of MINO plus NAC induces remyelination, this was seen with luxol fast blue staining. It is anticipated that MINO plus NAC will modulate inflammation, limit grey matter injury and induce remyelination when dosed beyond the 1-hour window. These data suggest that MINO plus NAC limits brain injury within a clinically useful therapeutic window. These preclinical studies provide further evidence that that MINO plus NAC has sufficient potency and safety to be tested against clinical TBI.

Andrew Wong

Advisor(s):David Schreiber

**Adjuvant radiation with hormonal therapy is associated with improved survival for men with pathologically involved lymph nodes following radical surgery for prostate cancer**

Rationale: Adjuvant hormonal therapy (aHT) is the standard treatment for prostate cancer patients found to have pathologically positive lymph nodes (pN+) at the time of radical surgery. Recent studies have suggested that the addition of adjuvant radiation therapy (aRT) to aHT may improve outcomes. The objective of this study was to assess the patterns of care and overall survival (OS) outcomes in men with pN+ prostate cancer using the National Cancer Data Base (NCDB). // Methods/materials: Men diagnosed with non-metastatic prostate cancer between 2004-2011 who underwent radical prostatectomy with at least one pathologically positive lymph node were identified in the NCDB. Patients were stratified into subgroups of those receiving no adjuvant therapy, aHT alone, aRT alone, and aRT + aHT. OS was analyzed via Kaplan Meier and compared between groups using the log-rank test. Multivariate Cox regression was used to identify covariates that impacted OS. // Results: A total of 7,225 patients were included in this analysis, of whom 3,636 (50.3%) received no adjuvant therapy, 2,041 (28.2%) aHT alone, 350 (4.8%) aRT alone, and 1,198 (16.5%) aRT + aHT. Five-year OS were 85.2% for no adjuvant therapy, 82.9% aHT alone, 88.3% aRT alone, and 88.8% combination aRT + aHT ( $p < 0.001$ ). On pairwise analysis, treatment with aRT + aHT was superior to no adjuvant therapy ( $p = 0.007$ ) and aHT alone ( $p < 0.001$ ) but not aRT alone ( $p = 0.44$ ). On multivariate analysis, aRT + aHT was associated with a significantly decreased risk of death (HR 0.67, 95%CI 0.54-0.82,  $p < 0.001$ ) compared to no adjuvant therapy whereas aHT alone (HR 1.04, 95%CI 0.89-1.21,  $p = 0.63$ ) and aRT alone (HR 0.96, 95%CI 0.70-1.32,  $p = 0.81$ ) were not. // Conclusion: Half of all men with pathologically positive lymph nodes after prostatectomy did not receive adjuvant therapy. However, patients treated with multimodal aRT + aHT had significantly higher OS than patients treated without adjuvant therapy or with aHT/aRT alone. /

Sylvia Wu

Advisor(s):Mariana Markell

**Late Post-Transplant Hypophosphatemia in an Inner City Population is Related to Insufficient Dietary Intake and Not Urinary Loss**

Hypophosphatemia is a common complication post-kidney transplant, and may contribute to ongoing bone loss and other complications. It has been ascribed to increased urine losses in the early post-transplant period. In our population, hypophosphatemia persists long-term, and the etiology is unclear. 15 randomly selected long-term patients were studied to examine factors that might influence phosphorus (PO<sub>4</sub>) levels, including diet estimated by 24 hour recall in face-to-face interview. The USDA Supertracker was used to estimate nutrient intake. / There were 9 women (60%), 11 Blacks (73%), and 14 (93%) who made <\$20K/yr. Mean patient (pt) age was 61.6+/-2.6, transplant (txp) age (yrs) 8.53+/-1.5, BMI 27.6+/-1.5, creatinine 1.5+/-0.3, intact PTH (iPTH) 113.5+/-26.1, Vit D 25.2+/-4.1, albumin 4.2+/-0.08, calcium 9.9+/-0.2, prot/creat ratio 0.93+/-0.5. Mean PO<sub>4</sub> was 2.94+/-0.16, 12 pts (80%) had plasma PO<sub>4</sub><3.5. Daily caloric intake was 1358.9+/-69.2, with 49% CHO, 21% protein and 30% fat. PO<sub>4</sub> intake (mg) was 1081.6+/-65.9, fractional excretion of PO<sub>4</sub> (FePO<sub>4</sub>) was 0.18+/-0.03 with random urine PO<sub>4</sub> 49.2+/-9.3. Plasma PO<sub>4</sub> correlated with BMI (r=0.68, p<0.05), calcium (r=-0.6, p<0.05), albumin (r=-0.5, p<0.05), but not FePO<sub>4</sub>, dietary PO<sub>4</sub>, caloric intake, creat, iPTH, Vit D or any other values. Diabetics did not differ from non-diabetics. / We conclude in our population of inner-city post-kidney transplant patients: 1. Hypophosphatemia is common and is worse in patients with lower BMI and albumin, but does not relate to iPTH or Vit D level. 2. Low FePO<sub>4</sub> suggests urinary losses are not responsible. 3. Although meeting the RDA for PO<sub>4</sub>, the correlation of lower BMI and albumin and low FePO<sub>4</sub> suggests nutritional factors play a major role. 4. Further investigation should determine whether persistent hypophosphatemia is due to dietary intake inadequate to replete early phosphate losses or whether other factors play a role in the indigent predominantly African-American population.

Jin Zhou

Advisor(s):Daniel Rosenbaum and Frank Barone

**GSK360A Inhibition of Prolyl 4-Hydroxylase in Ischemic Stroke: HIF Transcriptional Activation, Brain Protection and Reduced Sensory, Motor and Cognitive Deficits**

Since GSK360A upregulates systems in ischemic tolerance, its administration prior to surgery/ischemia could be beneficial in protecting organs, including the brain. Male Sprague Dawley rats received 2 hours transient middle cerebral artery occlusion followed by 22 hours of reperfusion. Vehicle (1% Methyl cellulose) or an optimum dose of GSK360A (30 mg/kg, p.o.) was administered and measurements were made of GSK 360A plasma, kidney and brain levels. Based on these data, GSK360A was then administered at 18 and 5 hour prior to stroke. The modified neurological severity score (mNSS), and individual measurements of sensory, motor, balance beam, foot fault and hind limb behavioral performance were made at 5 hour, 1 day, 1 week and 3 weeks after stroke. Cognitive performance (Active Place Avoidance; APA) was measured 3 weeks after stroke. In order to monitor exposure, GSK360A pharmacodynamic effects included kidney and brain erythropoietin (EPO) and Vascular Endothelial Growth Factor (VEGF) mRNA changes and plasma EPO and VEGF protein levels were made at 5 hours and 1 day after stroke. In addition, verification and measurement of terminal brain infarction was made at 4 weeks. GSK360A exhibited significant oral availability (plasma levels reached 7734 ng/ml) with significant kidney penetration (45-52%) but much less brain penetration (1-4%). GSK360A significantly increased kidney EPO mRNA >80-fold and increased Kidney VEGF mRNA >2-fold. The increased mNSS was significantly reduced by GSK360A (-46.5% at 1 week and -63.6% at 3 weeks after stroke). The performances in balance beam, foot fault and hind limb were all improved by GSK360A in a manner that increased more over time post-stroke. Deficits in stroke-induced cognitive dysfunction measured by APA were reduced by GSK360A without affecting motor activity. GSK360A also reduced brain infarction (30%, p<0.05). These data indicate that pre-stroke oral administration of GSK360A can provides brain protection.

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