Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

1 **Abstract Title: Tunable Release of Doxorubicin from PEG-poly(amino acid) Micelles**

Author(s): A. Ponta, College of Pharmacy, Department of Pharmaceutical Sciences, U of Kentucky
Y. Bae, College of Pharmacy, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:
PURPOSE: To develop a drug delivery system in the form of polymeric micelles based on poly(ethylene glycol)-poly(amino acids) block copolymers in order to achieve pH-dependent drug release in solid tumors in tunable manners. EXPERIMENTAL METHODS Block copolymers composed of PEG-poly(aspartate) containing 5, 15 or 35 aspartate repeating units were synthesized. These were subsequently modified with spacers [methyl-4-aminobenzoate (ABZ) or glycine methyl esters (GLY)]. Methyl esters were removed by introducing hydrazide. Resulting block copolymers were conjugated with doxorubicin (DOX). Micelles were prepared and thereafter characterized. DU-145 was used for in vitro cytotoxicity assays comparing free drug to the micelles. RESULTS Six different block copolymer containing different drug binding linkers were successfully synthesized. 1H-NMR was used to confirm each step of the process. Micelle particle size ranged from 20-50nm with a drug loading content from 2.8 to 31.0 weight percent. Drug release experiments indicated that modified micelles were pH-dependent and tunable. Introducing different spacers (Gly or Abz) played a key role in the drug release due to differing electron groups. Micellar efficacy was compared to free DOX through in vitro studies. Gly micelles had similar IC50s to free DOX, excluding ones with 35 repeating units. Abz micelles showed slightly higher IC50 concentrations than DOX. Intriguingly, Abz micelles had a higher IC50 value than the Gly micelles even though Abz micelles released more DOX, at a faster rate. This is attributed to importance of scheduled release. CONCLUSION A promising drug delivery platform based on PEG-poly(amino acids) has been developed for effective cancer treatment.

Supported by: Kentucky Lung Cancer Research Program
Primary Presenter / e-mail: Ponta, A. / andrei.ponta@uky.edu
Mentor or Senior Author / e-mail: Bae, Y. / younsoo.bae@uky.edu

2 **Abstract Title: Catabolic Response of C2C12 Myotubes Following Doxorubicin Exposure**

Author(s): L. A. A. Gilliam, Department of Physiology, U of Kentucky
J. S. Moylan, Department of Physiology, U of Kentucky
E. W. Patterson, Department of Physiology, U of Kentucky
Z. Rabbani, Department of Physiology, U of Kentucky
A. S. Wilson, Department of Physiology, U of Kentucky
J. D. Smith, Department of Physiology, U of Kentucky
M. B. Reid, Department of Physiology, U of Kentucky

Abstract:
Doxorubicin, a commonly prescribed chemotherapeutic agent, causes skeletal muscle wasting in cancer patients undergoing chemotherapy. Doxorubicin increases oxidants and decreases skeletal muscle mass in vivo. The purpose of this study was to investigate the cellular response of doxorubicin in vitro. We hypothesized that doxorubicin causes a catabolic response in C2C12 myotubes, increasing ROS and promoting atrophy. Cultured myotubes were exposed to doxorubicin (0.2 μM, 2-48 hrs). Cytosolic oxidant activity was measured using the redox sensitive probe dichlorofluorescin. We used real time PCR and Western blot to measure mRNA and protein for ubiquitin ligases MAFbx/atrogin-1 and MuRF1, the caspase-3 protease, and myofibrillar proteins actin and myosin. Oxidant activity was elevated 13 ± 9 % (2 hrs, n=18, $p<0.05$). Following doxorubicin (48 hrs) actin (-49 ± 4 %, n=3, $p<0.01$) and myosin (-40 ± 9 %, n=11, $p<0.05$) proteins were decreased. Doxorubicin increased MAFbx/atrogin-1 mRNA 16 and 24 hrs (74 ± 8%, n=3, $p<0.01$; 132 ± 8 %, n=3, $p<0.01$) following exposure, and elevated protein at 24 hrs (15 ± 4 %, n=13, $p<0.05$). Doxorubicin did not alter MuRF1 mRNA or protein (data not shown). Caspase-3 precursor and active form were elevated 6 hrs (precursor: 25 ± 7 %, n=3, $p<0.05$; active: 125 ± 35 %, n=3) and 24 hrs (precursor: 36 ± 6, n=3, $p<0.01$; active: 87 ± 12 %, n=3, $p<0.01$) following doxorubicin. Our data suggest that doxorubicin increases oxidants, leading to downstream catabolic signaling.

Supported by: NIH award: T32 HL086341-02(EWP), AHA 09PRE2020088 (LAAG), and the University of Kentucky College of Medicine
Primary Presenter / e-mail: Rabbani, Z. / zrabb2@uky.edu
Mentor or Senior Author / e-mail: Reid, M. B. / mbreid2@uky.edu

3	**Abstract Title:**	**Cross-linked Nanoassemblies (CNAs) of Poly(ethylene glycol)-poly(amino acid) Block Copolymers Designed as Stability-improved Drug Carriers**

Author(s): H. Lee, Department of Pharmaceutical Sciences, U of Kentucky
Y. Bae, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:

Introduction: Self-assembling block copolymer micelles have been used as drug carriers extensively because their small size of 20 - 100 nm and well-defined core-shell structure allow tumor-preferential drug delivery. However, in vivo stability of polymer micelles still needs to be improved to avoid micellar dissociation during dilution in the blood after injection. To resolve the concentration-dependent instability, we have designed a cross-linked nanoassemblies (CNAs) of poly(ethylene glycol)-poly(aspartic acid) [PEG-p(Asp)] block copolymers as stability-improved drug carriers. Experimental: PEG-p(Asp) block copolymer and 1,6-hexanediaine (HDA) were dissolved in DMSO and added with NHS, DIC, and DMAP. Cross-linking reaction was carried out at room temperature for 2 days. Synthesis was confirmed by NMR and GPC. Results and Discussion: CNA (~100 kDa) with crosslinking degree of 28 % appeared to consist of 11 block copolymers. The number of aspartic acids in each CNA was calculated as 253. It is noted that the concise and effective synthesis, crosslinking of PEG-p(Asp) block copolymer by HDA, resulted in CNA with desirable molecular properties such as multiple well-defined block copolymers and high number of aspartic acids as drug binding sites. Stability of CNA was evaluated by monitoring particle sizes and scattering intensities of CNA and PEG-p(Asp-Ca2+) micelle in comparison during dilution. It was demonstrated that crosslinking improves the stability of block copolymer-based nanoparticles as drug carriers. Conclusion: CNA was successfully prepared as stable and feasible drug carriers through crosslinking of PEG-p(Asp) block copolymers with diamine crosslinkers. CNA showed improved stability and considerable cargo capacity for drug payloads.

Supported by: Kentucky Lung Cancer Research Program
Primary Presenter / e-mail: Lee, H. / hjin.lee99@uky.edu
Mentor or Senior Author / e-mail: Bae, Y. / younsoo.bae@uky.edu

4	**Abstract Title:**	**Entrapment of Doxorubicin by PEG-poly(aspartate) Block Copolymers Influenced by Different Core Environments**

Author(s): A. Eckman, Pharmaceutical Sciences, U of Kentucky
A. Ponta, Pharmaceutical Sciences, U of Kentucky
Y. Bae, Pharmaceutical Sciences, U of Kentucky

Abstract:

Purpose: To evaluate biological and physiochemical properties of PEG-poly(aspartate) [PEG-p(Asp)] block copolymer micelles ionically entrapping doxorubicin hydrochloride (DOX). Methods: PEG-p(Asp) was synthesized from 5 kDa PEG and 20 Asp units. The carboxyl groups of p(Asp) were present as benzyl ester [PEG-p(Asp/Bz)], sodium salt [PEG-p(Asp/Na)] or free acid [PEG-p(Asp/H)]. The three block copolymers were mixed with DOX at various mixing ratios for polymer micelle preparation. Drug loaded micelles were then characterized to determine drug loading, particle size and release patterns. Cytotoxicity was evaluated using prostate (PC3 and DU145) and lung (A549) cancer cell lines. Results: DOX entrapment was 1.1, 56.8 and 40.6 wt % of DOX for PEG-p(Asp/Bz), PEG-p(Asp/Na) and PEG-p(Asp/H), respectively. Particle size for all micelles was < 100 nm. Micelles showed a time-dependent release of DOX in both pH 7.4 and 5.0 however, that release was accelerated in pH 5.0. The best stability was seen in PEG-p(Asp/Na) micelles at pH 7.4, retaining 31.8% of initial DOX for 48 h. Cytotoxicity of PEG-p(Asp/Na) micelles was over 20% more effective than free DOX in all three cell lines (PC3, DU145 and A549). Conclusion: Micelles containing an ionic core appear to be efficient in the entrapment of DOX. PEG-p(Asp/Na) micelles possessing counter ions appear to be the superior delivery method in that they are stable, release drugs for prolonged times in a pH-dependent manner, and suppress cancer cells effectively.

Supported by: Kentucky Lung Cancer Research Program
Primary Presenter / e-mail: Eckman, A. / allison.eckman@uky.edu
Mentor or Senior Author / e-mail: Bae, Y. / younsoo.bae@uky.edu

5 **Abstract Title: Polymer Micelles for Controlled Inhibition of Glycolytic Pathways in Tumors**

Author(s): S. Akter, College of Pharmacy, Pharmaceutical Sciences, University of Kentucky
H. J. Lee, College of Pharmacy, Pharmaceutical Sciences, University of Kentucky
Y. Bae, College of Pharmacy, Pharmaceutical Sciences, University of Kentucky

Abstract:
Background: Small molecule, 3-(3-pyridinyl)-1-(4-pyridinyl)-2-propen-1-one (3PO), is previously identified as a potent drug to inhibit transporters that are crucial for glucose update in cancer cells.We hypothesize that polymer micelles, nano-scaled drug carriers, will achieve controlled inhibition of glycolytic pathways in tumor tissues by delivering 3PO to solid tumors preferentially. The purpose of this study is to develop polymer micelles, nano-scaled drug carriers that can deliver 3PO to tumor tissues selectively, achieving drug release in a pH-controlled manner. Methods: Poly(ethylene glycol)-poly(aspartate hydrazide), comprising PEG (5 or 12 kDa) and aspartate (33-35 repeating units) were prepared, followed by conjugation of 3PO to the block copolymers through hydrazone bond. Characterization (particle size measurement) of the polymer micelles was done. Drug release patterns were observed under sink conditions at pH 7.4 and 5.0, 37°C, for 48 h. Results: 3PO loading yields were 2.08 wt% and 2.20 wt% for 12-35 polymer and 5-33 polymer respectively per each polymer chain. Polymer micelles entrapped with 3PO were 259 nm and 38 nm for 12-35 polymers and 5-33 polymers respectively.The micelles with 12 kDa PEG released 3PO more quickly at both pH 7.4 and 5.0 than the micelles with shorter 5 kDa PEG. Conclusions: The results demonstrate that polymer micelles successfully entrapped 3PO and released the drug in a controlled manner at different pHs. The polymer micelles would be useful to achieve a safe and effective therapy for lung cancer.

Supported by: Kentucky Lung Cancer Research Program
Primary Presenter / e-mail: Akter, S. / sak222@uky.edu
Mentor or Senior Author / e-mail: Bae, Y. / younsoo.bae@uky.edu

6 **Abstract Title: Stem Cell Factor Partially Rescues Albinism in a Murine Model of Humanized Albino Skin**

Author(s): J. P. Lagrew, University of Kentucky College of Medicine
P. Murapa, University of Kentucky College of Medicine, Department of Pediatrics and the Markey Cancer Center
J Vanover, University of Kentucky College of Medicine, Department of Pediatrics and the Markey Cancer Center
J. A. D'Orazio, University of Kentucky College of Medicine, Department of Pediatrics and the Markey Cancer Center

Abstract:
I Background- Oculocutaneous albinism (OCA) is a disorder of pigmentation with broad-ranging medical and psychological sequelae. The molecular defect in OCA involves loss of function of any one of a number of melanin synthetic enzyme in melanocytes, the neural crest-derived skin cells responsible for pigment production. OCA-1, the most common type of OCA, involves loss of function of the enzyme tyrosinase, which catalyzes the first two biosynthetic reactions in melanogenesis. Individuals affected by OCA are intensely sun-sensitive as a result of melanin deficiency. Besides being easily sunburned, such persons are at a very high lifelong risk of basal cell and squamous cell keratinocyte neoplasias. A murine model for the study of albinism was developed on the C57BL/6J background with mice that are defective at the tyrosinase locus. Whereas wild type C57BL/6 mice are intensely pigmented, their Tyrc2j/c2j counterparts lack epidermal melanin pigment and are, as a result, exceptionally UV-sensitive. It was previously believed that these mice were incapable of producing pigment; however, our lab demonstrated that C57BL/6 Tyrc2j/c2j mice that constitutively express stem cell factor (SCF) in the epidermis develop pigmentation in the ears, footpads, and tails as they age. This result suggested that the SCF signal cascade via the c-kit tyrosine kinase signaling cascade is capable of rescuing pigment production in the albino model. The present study hopes to further elucidate the molecular relationship between SCF and stabile tyrosinase expression. In particular, we are interested in the contribution of microphthalmia (Mitf), a transcription factor known to control melanogenesis, in SCF-mediated tyrosinase rescue. II Methods- The present study utilized B16 transformed murine melanocytes cultured in vitro. Stem Cell Factor treatments were applied to the cells at varying time points and concentrations and Tyrosinase and MITF expression were analyzed by Western Blot. Tyrosinase induction in the presence of MITF siRNA was also evaluated by Western Blot. III Results-SCF treatment induced a dose-dependent increase in levels of MITF as well as Tyrosinase in B16 melanoccytes. SCF was less effective at inducing tyrosinase expression in the presence of MITF siRNA. IV Conclusions- Stem cell factor, independent of Mc1r function, can induce tyrosinase expression via the c-kit pathway and MITF. The eventual application of this research would be a therapy for albinism that would target the c-kit tyrosine kinase and rescue eumelanin production, lowering morbidity and mortality associated with UV damage.

Supported by: R-01 grant from the National Cancer Institute
Primary Presenter / e-mail: Lagrew, J. P. / james.lagrew@uky.edu
Mentor or Senior Author / e-mail: D'Orazio, J. A. / jdora2@email.uky.edu

7	**Abstract Title:**	**Potential Role of Sphingosine-1 Phosphate Receptors in the in vivo Mobilization of Human Bone Marrow Derived Non-Committed Cells**

Author(s):
A. Karapetyan, Department of Internal Medicine, U of Kentucky
G. E. Van Zant, Departments of Internal Medicine, Hematology and Bone Marrow Transplantation
R. Hill, Departments of Internal Medicine, Hematology and Bone Marrow Transplantation
S. S. Smyth, Departments of Internal Medicine, Physiology and Pharmacology, U of Kentucky
A. Abdel-Latif, Department of Internal Medicine, U of Kentucky

Abstract:
Background: The bone marrow (BM) homes a multitude of pluripotent and partially committed stem cells that aid in the repair of various organs. The mechanisms underlying the mobilization and homing of these stem cells to injured tissues are poorly understood. Sphingosine-1 phosphate (S1P) and its receptors (S1PRs) are hypothesized to play an important role in this mobilization and/or homing. Procedures: We examined non-committed and CD34+ stem (NC) cells from non-mobilized human BM (hBM) (N = 3), human cord blood (hCB) (N = 3) and G-CSF mobilized human peripheral blood (hPB) (N = 3) for the expression of the mobilizing S1PR1, 3, 5 as well as intensity of their expression using flow cytometry. Results were analyzed using one way ANOVA and presented as percentage of NC cells expressing S1PRs (mean ± SEM). Results: The expression of S1PR1 and S1PR5 were significantly higher on hCB cells as compared to either hBM or hMPB NC cells (S1PR1: 1.4 ± 0.3 vs. 0.1 ± 0.02 vs. 0.3 ± 0.04, respectively; P = 0.0002 and S1PR5: 3.7 ± 0.9 vs. 0.3 ± 0.02 vs. 1.9 ± 0.6, respectively; P < 0.0001). Similarly, the expression of S1PR3 was significantly higher in hCB as compared to hMPB but not hBM NC cells (2 ± 0.7 vs. 0.3 ± 0.03 vs. 1.8 ± 0.6, respectively; P < 0.0001 for hCB vs. hMPB). Additionally, the median fluorescence of S1PR1 and S1PR5 were significantly higher in hCB and hMPB NC cells indicating higher surface receptor concentration. Conclusions: S1PRs show differentially higher expression on mobilized NC BM cells which is influenced by mobilization scenario. This supports a potential role of S1PRs in the mobilization of BM cells in vivo which can be potentially exploited in future studies exploring BM mediated tissue regeneration.

Supported by: UK Center for Clinical and Translational Science Pilot Award
Primary Presenter / e-mail: Abdel-Latif, A / akabde2@uky.edu
Mentor or Senior Author / e-mail: Smyth, S. S. / ssmyt2@uky.edu

8	**Abstract Title:**	**Glioblastoma Outcomes Differ According to Degree of EGFR Amplification in a Prospective Cohort**

Author(s):
J. Hobbs, College of Medicine, U of Kentucky
K. Cieply, Department of Pathology, U of Pittsburgh
R. Hamilton, Department of Pathology, U of Pittsburgh
C. Horbinski, Department of Pathology, U of Kentucky

Abstract:
Introduction: Glioblastomas (GBMs) are the most common and lethal primary brain tumor in the adult population. Many GBMs feature amplification of the Epidermal Growth Factor Receptor gene (EGFR), a powerful oncogene residing on chromosome 7 that is known to promote proliferation, radioresistance, and invasiveness. Fluorescence in situ hybridization (FISH) is the most common method to assess for EGFR amplification; most laboratories regard 2 or more copies of EGFR per copy of chromosome 7 (Chr 7) as amplification. Although many studies have been published on EGFR amplification and its impact on GBM biology, none have rigorously determined whether the proper EGFR:Chr7 cutoff ratio is truly 2, nor have any studies examined whether the amount of EGFR amplification might alter the clinical course. Experimental procedures: We prospectively analyzed a series of 819 gliomas with EGFR FISH, 542 of which were GBM, using overall survival as the primary endpoint. Results: Examining EGFR:Chr7 ratios in all gliomas suggested that 2 was indeed an appropriate cutoff point for amplification. There was a positive correlation between amplification and WHO grade (P < 0.0001). EGFR amplification also correlated with reduced survival time in all gliomas (P < 0.0001), but not in GBMs alone (P = 0.28). Remarkably, however, splitting the EGFR-amplified GBMs according to degree of amplification showed two subtypes: those with EGFR:Chr7 ratios between 2 and 20 had the shortest survival (median survival 0.62 years), followed by non-amplified GBMs (0.71 years) and amplified GBMs with a ratio over 20 (0.92 years) (P = 0.005) (Figure 1). Neither age nor amount of EGFR protein expression (as assessed by immunohistochemistry) accounted for this survival difference. Conclusions: These results suggest that, while a ratio of 2 is a justifiable cutoff, the biology of EGFR-amplified tumors is not homogeneous. This is the first study to identify this phenomenon. Additional work will be aimed at identifying the cause of this difference, as well as whether similar differences exist among other common neoplasms characterized by oncogene amplification (e.g. Her2-neu in breast carcinoma, EGFR in lung adenocarcinoma, and MYC in medulloblastoma).

Supported by: UK College of Medicine Physician Scientist grant
Primary Presenter / e-mail: Hobbs, J. / jghobb2@uky.edu
Mentor or Senior Author / e-mail: Horbinski, C. / craig.horbinski@uky.edu

9 **Abstract Title: College Sorority Members' Knowledge and Behaviors Regarding Human Papillomavirus and Cervical Cancer**

Author(s): M.E. Aleshire, College of Nursing, U of Kentucky

Abstract:

Introduction: Young people ages 15-24 acquire nearly one half of all new sexually transmitted diseases (STDs), and cervical human papillomavirus (HPV) is the most common STD in college age women. HPV prevalence in the United States is highest among sexually active females ages 14-24, and the incidence of genital HPV is higher in female college students than in many other populations. There is no known research that has examined sexual and health behaviors in female college sorority members to see if there is any correlation between such behaviors and knowledge of HPV and cervical cancer in this population. The purpose of this study was to discover female college sorority members knowledge regarding HPV and cervical cancer, to identify sexual risk behaviors in this group, and to ascertain if there is any relationship between knowledge of HPV and cervical cancer and sexual risk behaviors in this population. Method(s): A 24-item survey containing questions about HPV and cervical cancer knowledge and related risk behaviors was completed anonymously online by a convenience sample of 248 female college sorority members at a southern university. Descriptive statistical analysis was used develop an overall behavioral and knowledge profile for this group. ANOVA, Spearman's Rank Correlation, and independent t-tests were utilized to assess for relationships between HPV and cervical cancer knowledge and sexual and health behaviors in this group. Results: Female college sorority members demonstrated high-risk sexual behaviors and relatively low knowledge levels regarding HPV and cervical cancer. Knowledge scores in this group had no relationship to age, sexual relationship status, number of sexual partners, use of condoms, use of oral contraceptives, use of cigarettes, frequency of Pap tests, or personal or family history of HPV or cervical cancer. Discussion & Conclusions: Further research regarding HPV and cervical cancer, including randomized control trials needs to be implemented in college females. Healthcare providers and educators need to be aware of the significance of HPV in college females and promote healthy sexual behaviors and sexually transmitted disease education and HPV vaccination for college females.

Primary Presenter / e-mail: Aleshire, M. E. / mollie.aleshire@uky.edu
Mentor or Senior Author / e-mail: Lock, S. E. / selock0@email.uky.edu

10 **Abstract Title: Adolescent/Young Adult Cancer Survivors' Experiences of Connectedness with Their Healthcare Providers**

Author(s): C. Phillips-Salimi, College of Nursing, U of Kentucky
J.E. Haase, School of Nursing, Indiana U, Indianapolis, IN

Abstract:

Connectedness with healthcare providers (HCPs) is important to diminish risk-taking behaviors and improve health outcomes in adolescents and young adults with cancer (AYA). Little is known about experiences of connectedness with HCPs from perspectives of AYA. The purpose of this study was to describe AYA experiences of connectedness with HCPs across the cancer continuum. Empirical phenomenology, a qualitative method used to describe the essential commonalities of an experience across participants, was used to examine connectedness. The sample of nine young adult cancer survivors (ages 20-23 years) diagnosed in adolescence participated in in-person audio-taped individual interviews. Data analysis, using Colaizzi's method, involved systematic extraction of significant statements, meaning formulation, theme identification and comparison across participants. Trustworthiness and credibility strategies included peer checks, audit trail, and detailed description of findings. Seven theme categories indicate connectedness with HCPs is multi-faceted, encompassing experiences of connectedness, unconnectedness, and disconnectedness. There are three critical time points when connectedness can be fostered, hindered, and/or altered: at diagnosis, AYA acceptance of the reality of having cancer, and after treatment ends. Strategies that foster AYA connectedness were identified. HCP behaviors that foster unconnectedness or disconnectedness relate to lack of interest in and/or disrespect for AYA personhood. AYA-HCP connectedness fosters long-term care partnerships and may promote self-management during survivorship. Lack of connectedness or disconnectedness may lead to reluctance to connect with HCPs for cancer prevention. Knowledge obtained from this study can guide the development of interventions to enhance AYA-HCP connectedness that ultimately improve AYA survivorship.

Supported by: F31 Individual National Research Service Award, NIH/NINR (NR009733-01A1) T32 Training Grant, Institutional National Research Service Award, NIH/NINR (NR07066) American Cancer Society, Doctoral Degree Scholarship in Cancer Nursing (DSCN-05-181-01) MaryMargaret Walther Cancer Institute, Behavioral Oncology Cooperative Group - Pre-Doctoral Fellowship

Primary Presenter / e-mail: Phillips-Salimi, C. / cphillips-salimi@uky.edu
Mentor or Senior Author / e-mail: Haase, J. / johaase@iupui.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

11 **Abstract Title: Assessing the ABCD Screening Tool: Time for a Change?**

Author(s): M.T. Chung, University of Kentucky College of Medicine
R.L. Conigliaro, Department of Internal Medicine, University of Kentucky
S. Tobin, Department of Surgery, University of Kentucky

Abstract:

Introduction: In 1985, the ABCD screening tool (A-asymmetry, B-border irregularity, C-color variegation, D-diameter > 6 mm) was developed as a guide for patients to identify suspicious nevi. Its diagnostic accuracy has been questioned, as there are a growing number of small-diameter melanomas < 6 mm. With the current "D" parameter, small-diameter melanomas may be overlooked. Nodular melanomas, in particular, often do not meet any of the current screening criteria. Methods: A Medline search combining keywords 'ABCD criteria' and 'melanoma' generated 45 articles. Of those, 13 articles were identified that examined the ABCD screening tool. Five additional relevant articles were found via related citations of these. All searches were limited to articles in English language and to studies on humans. Results: Changes in a pigmented nevus may be the earliest sign of melanoma. In one study, family doctors identified changes in size, shape, and color in 94, 95, and 89 of 100 suspicious pigmented lesions being analyzed, respectively. All biopsy-confirmed melanomas were noted to have at least one of these dynamic features, prior to referral. Another retrospective study surveyed 125 patients after they had been diagnosed with melanoma; 78.1% of patients with nodular melanoma and 71.4% of patients with superficial spreading melanoma reported a change in the appearance of their lesion. In a third retrospective study of 429 patients with biopsy-confirmed melanoma, the top three features patients reported noticing were change to a darker color (58.3%), increase in size (41.3%), and increase in elevation of a pigmented lesion (19.8%). A screening tool for patients should be simple and easy to use. Girardi et al. compared the effectiveness of educating patients on melanoma detection for ten minutes, using either the ABCD criteria or photographs to describe patterns. Patients were tested on their ability to distinguish benign nevi from melanoma before the education and again one week after. Education with photographs was found to be superior. The darkness of a pigmented lesion is an important factor in diagnosis. One study objectively evaluated 53 melanomas and 142 non-melanoma lesions using a telespectrophotometric method based on measurements of lesion reflectance. This study found that melanomas had a significantly darker hue (minor reflectance) than benign nevi; this feature was critical in distinguishing the two. Conclusion: It has been shown that patients rely on changes in moles to raise suspicion. Humans use pattern recognition to process the visual world, a strategy dermatologists rely on to distinguish benign from malignant lesions. We propose educating the public with a screening tool consistent with this natural process, similar to what dermatologists use. We suggest a new screening tool: Triple D (DDD): Dynamic (changing), ugly Duckling (pattern recognition), and Dark (color).

Supported by: Summer Research

Primary Presenter / e-mail: Chung, M. T. / mike.chung@uky.edu
Mentor or Senior Author / e-mail: Conigliaro, R. L. / rlconi2@email.uky.edu

12	**Abstract Title:**	**Evaluation of Repeat Brachytherapy for Management of Localized Prostate Cancer Recurrence**

S. J. Campbell, U of Kentucky Dept. of Radiation Medicine
R Rowland, U of Kentucky Dept. of Biostatistics
Author(s): B. Shelton, U of Kentucky Division of Urology
P. H. Shah, U of Kentucky Dept. ofRadiation Medicine
W. H. St. Clair, U of Kentucky Dept. of Radiation Medicine

Abstract:

Purpose/Objective(s): Despite the enormous success of prostate brachytherapy for the treatment of prostate cancer, there is little data regarding treatment options for patients who experience a biochemical failure without distance metastases. We retrospectively evaluated the outcome of prostate cancer patients who were initially treated with brachytherapy, followed by salvage brachytherapy for biochemical failure. Material/Methods: From 2/2001 through 9/2010, 18 patients were identified as having a localized prostate cancer failure and were retreated by interstitial brachytherapy. All patients eligible for a second brachytherapy procedure exhibited a PSA nadir followed by three successive rises or a PSA rise greater than 2 ng/ml above the nadir value. All patients underwent a bone scan as well at a CT of the abdomen and pelvis to rule out metastasis. The CT scan was also used to assess the seed distribution in the prostate from the previous brachytherapy procedure. The CT scan in combination with a transrectal ultrasound was used to generate a PTV for focal prostate brachytherapy. Men with excellent seed distribution from their first brachytherapy procedure were not eligible for a second implant. Results: Prior to the initial treatment Gleason scores ranged from 3 to 7, median 6.0 and pretreatment PSA ranged from 3.1 to 19.1 ng/ml, median 6.67. Clinical T-stage was: T1c (8), T2a (6), T2b (3), and T2c (1). 12 patients had their initial brachytherapy at the University of Kentucky; six patients had their initial brachytherapy at other institutions. Median interval between the first implant and second implant was 74.3 months (19 to 288 months). Two patients experienced very late PSA failure after undergoing open brachytherapy procedures in the 1980s. Median pre-salvage PSA was 3.3 ng/ml and ranged from 0.98 to 17.41 ng/ml. All patients received salvage interstitial brachytherapy using 125I. Using the Phoenix criteria, we have 5 failures (28% failure rate). Median time to failure for these five patients was 18 months (12-95 months). Conclusion: Patients who have been treated for prostate cancer by interstitial brachytherapy may be eligible for salvage with additional brachytherapy. However the patients must be carefully selected for focal prostate seeding on the basis of the CT and ultrasound. Further investigation could be useful to develop patient selection criterion for salvage brachytherapy. These early results show salvage brachytherapy is an effective option for the management of patients who experience biochemical failure after primary interstitial brachytherapy. Longer follow-up is needed to confirm this outcome.

Supported by: University of Kentucky Dept of Radiation Medicine
Primary Presenter / e-mail: Campbell, S. J. / sjcamp4@uky.edu
Mentor or Senior Author / e-mail: St. Clair, W. H. / stclair@email.uky.edu

13	**Abstract Title:**	**Clinical Comparison of Posaconazole vs. Fluconazole Prophylaxis in Patients with Acute Myelogenous Leukemia or Myelodysplastic Syndrome**

B.J. Ereshefsky, Department of Pharmacy Services, University of Kentucky HealthCare
Author(s): C. Martin, Department of Pharmacy Services, University of Kentucky HealthCare
A.P. Lawson, Department of Pharmacy Services, University of Kentucky HealthCare

Abstract:

Purpose: Patients with acute myelogenous leukemia (AML) or myelodysplastic syndrome (MDS) receiving induction chemotherapy experience prolonged neutropenia, placing them at increased risk for invasive fungal infections. In 2007, posaconazole was found to be superior to fluconazole for fungal prophylaxis in these patients. However, posaconazole is available only as an oral suspension and has poor absorption if not taken with a high fat meal or supplement. In a real-world clinical environment it may be difficult to ensure adequate nutritional intake to maximize the drug's absorption. The purpose of this study was to evaluate antifungal resource utilization with each prophylactic regimen, which will serve as a surrogate endpoint for actual fungal infection. To that end, the primary objective of this study was to determine if posaconazole, as compared with fluconazole, decreased the utilization of subsequent antifungal agents such as micafungin, voriconazole, or amphotericin B. Secondary objectives will include time to first change of antifungal medication, antifungal-related adverse events, proven fungal infections, and mortality. Methods: This project was approved by the Institutional Review Board of the University of Kentucky. A retrospective chart review was conducted to include patients diagnosed with AML or MDS undergoing induction chemotherapy and receiving antifungal prophylaxis with either fluconazole or posaconazole. Relevant data were collected on all applicable patients > 18 years of age who were treated at University of Kentucky HealthCare between July 1, 2005 and September 1, 2010. The primary outcome will be evaluated using logistic regression, patient demographics will be evaluated using the chi-squared test, and secondary outcomes will be evaluated using the student t-test, Wilcoxon Rank Sum Test, the Cox proportional hazard, and Kaplan Meier Curves. Results: Results and conclusions to be presented at the Great Lakes Residency Conference.

Primary Presenter / e-mail: Ereshefsky, B.J. / b.ereshefsky@uky.edu
Mentor or Senior Author / e-mail: Martin, C. / craig.martin@uky.edu

14 **Abstract Title:** **Risk Factors for Adverse Outcome Following Skin-Sparing Mastectomy and Immediate Prosthetic Reconstruction**

Author(s):
E. M. Kobraei, University of Kentucky College of Medicine
J. Nimtz, Division of Plastic Surgery, University of Kentucky
L. Wong, Division of Plastic Surgery, University of Kentucky
J. Buseman, Division of Plastic Surgery, University of Kentucky
P. Kemper, Division of Plastic Surgery, University of Kentucky
H. Wright, Department of Surgery, University of Kentucky
B. D. Rinker, Division of Plastic Surgery, University of Kentucky

Abstract:
Background: A single-center retrospective study was conducted to identify risk factors for adverse outcomes following skin-sparing mastectomy and immediate prosthetic reconstruction. Few studies have attempted to define these risk factors and results are inconsistent, with no established selection criteria available. We identify patient and procedure-related characteristics that are predictive of unfavorable postoperative outcomes. Identification of such risk factors allows clinicians to apply rational preoperative screening measures to reduce postoperative complications. Methods: Postoperative complications and implant losses in 102 patients (155 breasts) were evaluated as outcomes. Major complications were defined as a breast-related return to the operating room or hospital admission. Minor complications included skin flap necrosis, hematomas, seromas, non-healing wounds, and culture proven surgical site infections. The six patient characteristics studied were age, smoking, BMI, diabetes mellitus, radiotherapy, and chemotherapy. The three procedural characteristics included use of acellular dermis, bilateral operation, and one-stage reconstruction with a permanent implant. Univariate logistic regression analysis was performed to assess potential risk factors. Results: The use of acellular dermis was associated with a greater than three-fold increased risk of postoperative complications ($p = 0.007$). None of the patient-related characteristics studied behaved as risk factors for postoperative complications, although radiotherapy exposure had a significant association with implant loss ($p = 0.04$). Conclusions: A cautious and conservative approach to using acelluar dermal matrix is warranted until its effect on postoperative outcomes is more clearly defined. Our data support findings from other studies of the deleterious effect of breast radiotherapy on postoperative outcomes.

Primary Presenter / e-mail: Kobraei, E. M. / emkobr2@uky.edu
Mentor or Senior Author / e-mail: Rinker, B. / brink2@email.uky.edu

15 **Abstract Title:** **Cyclooxygenase-2 inhibition attenuates progression of abdominal aortic aneurysms in mice by regulating the smooth muscle cell phenotype**

Author(s):
Kamalika Mukherjee, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
Charles D Loftin, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky

Abstract:
Abdominal aortic aneurysm (AAA) is a chronic inflammatory disease with no available pharmacological treatment. Human aneurysmal tissue is characterized by increased expression of cyclooxygenase-2 (COX-2). Similarly, in a mouse model of the disease induced by chronic Angiotensin II (AngII) infusion, we have shown that inactivation of COX-2 prior to disease initiation reduces AAA incidence. The objective of the current study was to determine the effectiveness of COX-2 inhibition after initiation of the disease. Mice were treated with or without celecoxib after beginning AngII infusion, and AAA development was analyzed at different time-points. The celecoxib treated mice had a significantly reduced incidence of AAAs and were protected from aortic rupture and death. The effectiveness of celecoxib was associated with significantly increased mRNA expression of markers of differentiated smooth muscle cell (SMC) phenotype including alpha-actin, SM22-aplha, desmin, myosin heavy chain 11 and smoothelin. Celecoxib treatment also decreased mRNA expression of a marker of dedifferentiated SMC (hyaluronic acid synthase 2). Similarly, in cultured aortic SMCs, celecoxib treatment increased expression of a marker of SMC differentiation. These findings suggest that COX-2 inhibition attenuates progression of AAAs by maintaining a differentiated phenotype in abdominal aortic SMCs.

Supported by: NIH, HL083122
Primary Presenter / e-mail: Mukherjee, K. / kmukh2@email.uky.edu
Mentor or Senior Author / e-mail: Loftin, C. D. / cdloft2@email.uky.edu

16	**Abstract Title:**	**Sphingomyelinase Causes Diaphragm Dysfunction Through Mitochondrial Oxidants**

Author(s):
S. A. Stasko, Department of Physiology, U of Kentucky
L. F. Ferreira, Department of Applied Physiology and Kinesiology, U of Florida, Gainesville, FL
L. A. Gilliam, Department of Physiology, East Carolina University, Greenville, NC
M.B. Reid. Department of Physiology, U of Kentucky

Abstract:
Patients with chronic heart failure have elevated plasma sphingomyelinase (SMase) activity and decreased skeletal muscle force production. In vitro administration of exogenous SMase to murine diaphragm depresses maximal force, accelerates fatigue, and stimulates reactive oxygen species (ROS) production. ROS mediates dysfunction induced by sepsis, mechanical ventilation and TNF exposure. However, a link between increased SMase activity, ROS production, and skeletal muscle dysfunction has not been established. We tested the hypothesis that SMase acts via mitochondrial oxidants to depress force and accelerate fatigue in the diaphragm. We studied in vitro force production by diaphragm muscle bundles from adult male mice (n=5). Muscles were incubated with Krebs-Ringer solution (control), SMase (0.5 U/ml), or SMase (0.5 U/ml) and SS-31 (100 μM); a specific inner mitochondrially targeted antioxidant) for 1 hr. We used a standard force-frequency protocol to assess muscle function after each treatment. Maximal force was depressed ($p<0.05$) in muscles treated with SMase (17.5±0.7 N/cm^2) compared to controls (24.1±0.4 N/cm^2) and SS-31 protected against the SMase induced depression of force in the diaphragm (SMase + SS-31 = 21.2±0.8 N/cm^2; $p>0.05$ vs. SMase). SS-31 antioxidant treatment also completely abolished the SMase effects of accelerated fatigue in diaphragm (Control = 2.8±0.5 N/cm^2, SMase = 2.1±0.4 N/cm^2, SMase + SS-31 =2.8±0.5 N/cm^2; $p>0.05$) Conclusion: Exogenous SMase administration causes diaphragm dysfunction and SS-31 treatment suppresses the SMase induced weakness. The mitochondrially targeted antioxidant suggests a mechanism of diaphragm dysfunction mediated through mitochondrially produced oxidants.

Supported by: NIH T32: Research Training in Muscle Biology of Cardiopulmonary Disease
Primary Presenter / e-mail: Stasko, S. A. / sastas2@uky.edu
Mentor or Senior Author / e-mail: Reid, M. B. / mbreid2@email.uky.edu

17	**Abstract Title:**	**CAL-120, an Orally Available Isoform Selective PI3K Inhibitor for the Potential Treatment of Advanced Non-Small Cell Lung Cancer (NSCLC)**

Author(s):
C.L. Westendorf, Pharmacy Services, UK HealthCare; College of Pharmacy, University of Kentucky*
K. Ratermann, College of Pharmacy, University of Kentucky*
C. Stamatkin, College of Pharmacy, University of Kentucky
J. Bryant, College of Pharmacy, University of Kentucky
B. Jones, PhD, College of Pharmacy, University of Kentucky
M. Milewska, MSPharm, College of Pharmacy, University of Kentucky
B. Lannutti, PhD, Calistoga Pharmaceuticals, Inc, Seattle, WA
E.P. Black, PhD, College of Pharmacy, University of Kentucky

Abstract:
Specific Aims: To test oral isoform-selective Phosphatidylinositol 3-kinase (PI3K) inhibitors in lung cancer cell lines and develop genomic signatures that predict response. Background: Lung cancer is the leading cause of cancer-related mortality in the US with an estimated 157,300 deaths in 2010. New therapeutic targets and agents are needed to improve patient outcomes. PI3K pathway is deregulated in lung cancer. We hypothesize that PI3K inhibitors will show activity in lung cancer and genomic signatures exist that will predict activity. Methods: NSCLC cell lines exposed to delta/beta PI3K inhibitor, CAL-120, was evaluated for cell proliferation, death, apoptosis, cell cycle effect, and signaling inhibition. Additionally, gene expression data were collected using Affymetrix U133 2.0 arrays. The data will be used to develop a predictive algorithm of response using published methods. Results: CAL-120 treatment resulted in reduction in cell growth in several cell lines, using effective concentrations of 5 and 10 μM. The greatest activity was seen in cell lines with K-Ras or Akt activation. Treatment with CAL-120 attenuated PI3K/Akt pathway signaling in sensitive cell lines at concentrations tested. We indentified 30 genes that predict response to CAL-120 in a training set and these genes are being validated in additional studies. Conclusion: The PI3K isoform-selective inhibitor, CAL-120, has a growth-inhibitory effect on some NSCLC cell lines, consistent with PI3K inhibition. We are currently validating a gene expression signature to predict response.

Supported by: Calistoga Pharmaceuticals, Inc, Seattle, WA
Primary Presenter / e-mail: Westendorf, C. L. / cwe226@uky.edu
Mentor or Senior Author / e-mail: Black, E. P. / Penni.Black@uky.edu

18 **Abstract Title:** **Digital Pulse Amplitude Testing of Endothelial Function in Pregnancy**

Author(s):
C.F. Pearce MD, Department of OB/GYN, Division of Maternal Fetal Medicine, U of Kentucky
M.J. Garabedian MD MPH, Department of OB/GYN, Division of Maternal Fetal Medicine, U of Kentucky
R.I. Epstein MD MBA, Department of OB/GYN, Division of Maternal Fetal Medicine, U of Kentucky
H-L. Duong MD, Department of OB/GYN, Division of Maternal Fetal Medicine, U of Kentucky
T.E. Curry PhD, Department of OB/GYN, U of Kentucky
W.F. Hansen MD, Department of OB/GYN, Division of Maternal Fetal Medicine, U of Kentucky
K.Y. Lain MD MS, Department of OB/GYN, Division of Maternal Fetal Medicine, Norton Healthcare, Louisville, KY

Abstract:
Background: Endothelial function can be tested non-invasively as flow mediated dilation (FMD) by brachial artery ultrasound or as the reactive hyperemia index (RHI) on endothelial pulse amplitude testing (Endo-PAT). Because RHI is a ratio of vascular dilation, the physiologic baseline vasodilation of pregnancy may invalidate this testing modality in pregnancy. Since cotinine (a known marker for smoking exposure) has been shown to correlate with FMD, we hypothesized cotinine should also correlate with RHI, if EndoPAT testing is reliable in pregnancy. Methods: Primigravidas (29 smokers, 31 non-smokers) at 16-22 weeks gestation were tested with the Endo-PAT2000 device (Itamar Medical Ltd. Caesarea, Israel). Age, body mass index (BMI), blood pressure (BP), heart rate (HR), and serum samples for cotinine and high sensitivity c-reactive protein (CRP) were obtained. Statistical analysis was done with SAS. Results: There was no difference in age, BMI, or mean RHI between groups. Cotinine did not correlate with RHI (r= -0.024, p=0.86). No difference in RHI was noted among those with low (<10), moderate (10-150), or high (>150) cotinine levels. RHI did correlate with HR (r= -0.42, p=0.0008) and BP(r= -0.38, p=0.0034), but not with CRP (as a marker of cardiovascular risk). Discussion: The data supports the concern that Endo-PAT does not accurately discriminate endothelial function in mid-gestation. Because Endo-PAT relies on measurement of volume changes in the digit, we speculate that the baseline dilation of peripheral vascular beds in pregnancy prevents this modality from demonstrating significant differences in RHI. Further study of Endo-PAT in pregnancy is needed.

Supported by: Department of OB/GYN, U of Kentucky
Primary Presenter / e-mail: Pearce, C. F. / christy.pearce@uky.edu
Mentor or Senior Author / e-mail: Lain, K. Y. / kristine.lain@gmail.com

19 **Abstract Title:** **Short-term Outcomes for Open Revascularization of Chronic Mesenteric Ischemia: A Comparison between Vein and Prosthetic Conduit**

Author(s):
D. L. Davenport, Department of Surgery, University of Kentucky
A. Shivazad, College of Medicine, University of Kentucky
E. D. Endean, Department of Surgery, University of Kentucky

Abstract:
Introduction: Surgical bypass as treatment for chronic mesenteric ischemia is performed to alleviate symptoms of weight-loss and postprandial pain and to prevent catastrophic intestinal necrosis. Few reports evaluate outcome with a focus on the type of conduit used for the bypass. The purpose of this study was to evaluate contemporary short-term outcomes of patients who underwent aorto-mesenteric bypass for chronic mesenteric ischemia. Methods: Data from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) Participant Use file was analyzed for demographic and clinical risk variables, mortality, and 22 defined complications (morbidity) between 2005 and 2009 from over 200 participating hospitals. The database was queried for patients undergoing aorto-mesenteric bypass with vein (CPT 35531) or non-vein (CPT 35631) whose preoperative diagnosis was chronic mesenteric ischemia (ICD-9 code 557.1). Outcomes and risk variables were compared using univariate analysis and independent sample t-tests for continuous variables. Results: One hundred fifty six patients underwent mesenteric revascularization; 119 (76%) women, 37 men (24%) with an average age of 65 ± 13 years. The conduit used was vein in 44 (28%) and prosthetic graft in 112 (72%). In patients with a vein graft, a higher percentage had a contaminated surgical site infection (30% vs. 7%, p = 0.001) and underwent emergent surgery more frequently (16% vs. 4%, p = 0.012). Mortality was higher in patients in which a vein graft was used (16% vs. 5%, p = 0.039). More patients undergoing bypass with vein had an associated bowel resection, sepsis, or SIRS and hyponatremia. There were no differences noted between the two groups in length of stay or post-operative complications, including infectious complications, renal insufficiency, myocardial infarction, and stroke. Moreover, there were no statistically significant differences between the two groups in mean age, smoking history, recent weight-loss, obesity (BMI >25) rates, length of operation, re-operation frequency, and early graft failure. Conclusions: Thirty day mortality was higher in patients who had vein used for mesenteric bypass. However, this group also had a higher incidence of emergent surgery, bowel resection, and contaminated operative field. This suggests that vein grafts were preferentially used in the face of bowel infarction. The higher mortality is likely due to other patient factors such as the extent of bowel ischemia at the time of operation, and outcomes may not be directly related to the type of conduit used. If expeditious revascularization is done prior to development of bowel infarction, vein or prosthetic conduit would be expected to function equally well.

Primary Presenter / e-mail: Shivazad, A. / shivazad@gmail.com
Mentor or Senior Author / e-mail: Endean, E. / edende0@email.uky.edu

20 **Abstract Title: Effect of Etomidate on Adrenocortical Suppression: A Review of Intubated Septic Patients**

Author(s):
M. L. Thompson, Department of Pharmacy, University of Kentucky HealthCare
K. A. Weant, Department of Pharmacy, University of Kentucky HealthCare
S. Baker, Department of Pharmacy, University of Kentucky HealthCare
E. Bensadoun, College of Medicine, Department of Pulmonary Critical Care, University of Kentucky HealthCare

Abstract:
Purpose: Etomidate is commonly used for the induction of anesthesia and during rapid sequence intubation in the critically ill population. Although desirable for its rapid and short-lived effects, etomidate can inhibit cortisol production in the adrenal cortex, potentially causing or exacerbating hypotension in susceptible patient populations. Septic patients are at increased risk of independently developing adrenal suppression and this has been associated with increased mortality in some studies. The use of etomidate in septic patients is controversial due to the effects on cortisol production, however data are still lacking to prove that etomidate should be avoided in this patient population. Our objective was to review septic patients who received etomidate during their intubation and determine if the drug is associated with worse outcomes when compared to those not receiving etomidate. The primary endpoint was clinically significant hypotension, defined as a systolic blood pressure <90 mmHg or a mean arterial pressure of <60 mmHg. Secondary endpoints included vasopressor use, corticosteroid use, days on mechanical ventilation, length of stay and mortality. Methods: A retrospective cohort study was conducted on patients intubated in the emergency department and on medical wards at the University of Kentucky Medical Center, a tertiary care academic medical center. Medical charts from patient visits were reviewed from 2005 to 2010. Patients were identified by a diagnosis of sepsis and requiring intubation, who received either etomidate during intubation or a different agent. It was estimated that 188 patients, 94 in each group, would be necessary to detect a 20% absolute difference between the two groups. Data collection included hemodynamic measurements before and after intubation, SOFA score at the time of intubation, vasopressor use, corticosteroid use, intensive care unit length of stay, hospital length of stay and mortality at 28 days. Results: Data collection is in progress.

Primary Presenter / e-mail: Thompson, M. L. / mth226@email.uky.edu
Mentor or Senior Author / e-mail: Weant, K. A. / kawean2@uky.edu

21 **Abstract Title: Evaluation of Sotalol in Veteran Affairs Patients with Renal Dysfunction**

Author(s):
C. J. Beavers, Cardiology, UK HealthCare
M. Lane, Lexington VA and U of Kentucky College of Pharmacy
B. Lea, Lexington VA
S. Elayi, Lexington VA and UK HealthCare Gill Heart Institute
T. Macaulay, AQ-Cardiology, UK HealthCare Pharmacy Services and Gill Heart Institute and U of Kentcky College of Pharmacy

Abstract:
BACKGROUND: Sotalol is a non-selective adrenergic blocking antiarrhythmic which, in addition to its beta blocking effects, has Vaughan Williams class III antiarrhythmic characteristics. Sotalol, marketed under Betapace, originally was approved for the treatment of sustained and unsustained ventricular arrhythmias. In 2000 it was approved for atrial fibrillation and flutter under the name Betapace AF. Due to its unique mechanism of action, sotalol can prolong the QTc interval and progress to torsades de pointes. Examination of the Betapace package insert provides a tiered dosing scheme for renal dysfunction, whereas the Betapace AF package does not have a cutoff below a creatinine clearance (CrCl) of 40mL/min. It is postulated lingering sotalol in renal disease produces a proarrhythmic state. The combination of renal disease, sotalol pharmacokinetics, adverse effects and the implications of this perfect storm of variables has only been highlighted in the literature as case reports, which lack the power to extrapolate to a population nor focuses on long term outcomes. The goal of this study was to examine Veteran Affairs (VA) patients who received sotalol with renal dysfunction to determine if the rate of morality and adverse events is greater compared to non-renally excreted amidodarone. METHODS: This was a retrospective database analysis using the VA's Veteran Integrated Service Network (VISN) 9 Data Warehouse. Patients were included if they were 18, had an ICD-9 code for atrial fibrillation, received a prescription for sotalol or amiodarone, had CrCl <60mL/min as calculated using the Cockcroft-Gault formula at time of sotalol or amiodarone initiation, and were in the Data Warehouse during February 2000 to June 2009. The primary outcome was death with secondary outcomes were development of other arrhythmias or adverse events. RESULTS: Results will be presented. CONCLUSIONS: Conclusions will be presented.

Primary Presenter / e-mail: Beavers, C. J. / cjbeav2@uky.edu
Mentor or Senior Author / e-mail: Macaulay, T. / temaca2@uky.edu

22 **Abstract Title:** **Adverse Cardiovascular Events due to Dopamine - A Comparison between Dopamine other Vasoactive Agents**

Author(s): K. Pandya, Department of Pharmacy Services
S. Baker, Department of Pharmacy Services
K. Weant, Department of Pharmacy Services
P. S. Winstead, Department of Pharmacy Services
J. Martin, Department of Emergency Medicine

Abstract:
Background: The cornerstone of therapy for the hemodynamic management of patients in cardiovascular shock is the administration of fluids, however this treatment modality is often insufficient. Norepinephrine and dopamine are both recommended as first line vasoactive agents for the management of fluid-refractory shock. Research comparing the efficacy of these two agents dates back to the 1970's, and none of these studies have shown a clinical difference as to which vasopressor is superior at shock management. However, studies have shown that the use of dopamine results in more adverse events than norepinephrine with the most common being arrhythmias. In addition, the Sepsis Occurrence in Acutely Ill Patients (SOAP) study found that dopamine administration was an independent risk factor for death in the intensive care unit. In the most recent trial comparing the two vasopressors, no difference in 28 day mortality was found between patients with shock that were treated with either norepinephrine or dopamine. Dopamine use, however, was associated with more adverse events than its comparator, most commonly presenting as arrhythmias. This is the largest study to date comparing the two vasopressors. The external validity of this study was significantly limitedby the fact that they excluded patients that had a history of a serious arrhythmia, such as atrial fibrillation or ventricular tachycardia. Objectives: To determine if the use of dopamine as a first line vasopressor at the University of Kentucky results in more adverse events than other vasopressors. A sub-group analysis will also be performed on patients with a past medical history significant for cardiovascular issues, particularly atrial fibrillation, given it is the most common tachyarrhythmia associated with dopamine. Time to administration of the vasopressor will also be reviewed to see if there is a significant delay associated with the preparation of norepinephrine in contrast to premixed dopamine. Study Design: A retrospective analysis of patients receiving vasopressor therapy (specifically, norepinephrine, vasopressin, dopamine or phenylephrine or any combination of the aforementioned) who presented to the emergency department (ED) from January 1, 2007 - July 30, 2010 will be conducted. Inclusion criteria include: adults greater than 18 years of age, patients who were admitted through the ED and who received vasopressor therapy. Exclusion criteria include: pregnancy. Outcomes: Data collection and evaluation is currently being conducted.

Primary Presenter / e-mail: Pandya, K. / kapa223@uky.edu
Mentor or Senior Author / e-mail: Baker, S. / stephnbaker@uky.edu

23 **Abstract Title:** **Cost Analysis of Short Acting Antihypertensive Therapy in Acute Care**

Author(s): C. P. Miller, College of Medicine, U of Kentucky
A. M. Cook, College of Pharmacy, U of Kentucky
A. C. Bernard, Department of Surgery, U of Kentucky

Abstract:
Purpose: Hypertension is common in hospitalized patients and there are many causes. Some patients have no history of hypertension, few symptoms and no apparent morbidity. Though there is no established guideline for therapy in these cases, patients often receive therapy directed at the abnormal vital sign. It is hypothesized that this practice is common and the associated costs are significant. Methods: Inpatient pharmacy database was queried at our University level I trauma and referral center. Patients on the emergency general surgery or orthopedic surgery services receiving IV hydralazine, metoprolol or labetalol were analyzed for indications, parameters, associated history of hypertension and direct costs. Results: Over the four month study period, 114 subjects were identified who received 522 drug administrations. 55% of subjects had a prior history of hypertension but only 75% were started on their home medication. Of those without hypertension prior to admission, only 18% required or received therapy at discharge. Only 13% received a diagnosis of hypertension at discharge. Labetolol was the most frequently used agent and total costs for this cohort of patients was over $1200. Conclusion: PRN, short-acting anti-hypertensive therapy has little evidence base in asymptomatic patients however its prevalence is high on surgical services. The cost is significant, especially when extrapolated to the larger hospital population at this single institution. Further research is warranted to determine the prevalence of this practice in other centers or national regions, as well as its cost and benefit.

Supported by: Professional Student Mentored Research Fellowship from UK Center for Clinical and Translational Science
Primary Presenter / e-mail: Miller, C. P. / cpmi222@uky.edu
Mentor or Senior Author / e-mail: Bernard, A. C. / acbern00@email.uky.edu

24	**Abstract Title:**	**Effect of Anti-fibrinolytic Prophylaxis on Post-operative Bleeding and Mortality During On-pump Cardiac Surgeries**

Author(s):
A. Koul, U of Kentucky College of Medicine
V. Ferraris, Department of Surgery, Division of Cardiothoracic Surgery, U of Kentucky
D. L. Davenport, PhD, Department of Surgery and Decision Science and Information Systems, U of Kentucky
C. Ramaiah, Department of Surgery, Division of Cardiothoracic Surgery, U of Kentucky

Abstract:
Background: Post-operative hemorrhage is a common complication of cardiac surgery. The purpose of this study was to compare post-operative bleeding and mortality rates in patients receiving two different anti-fibrinolytic agents, Aprotinin and Amicar, during cardiac surgeries. Methods: A retrospective chart review examined 523 subjects undergoing on-pump cardiac surgeries between January 2005 and May 2009. Multiple data points were collected including patient demographics, procedure performed, pre-operative risk factors, anti-fibrinolytic agent given, blood products transfused, 24-hour chest-tube output, cardiopulmonary bypass time, and ischemic time. Both univariate analysis and multivariable regression analysis of post-operative chest tube drainage was performed. Results: Post-operative bleeding rates varied significantly between patients receiving Aprotinin versus Amicar (P=0.001). Patients receiving Aprotinin bled on average 13% less than those receiving Amicar. There were a total of 17 deaths in the entire series (3.3%), the majority of who were high-risk patients. 11 deaths (3.3%) occurred in the Amicar group and 6 (3.2%) occurred in the Aprotinin group. There was no significant difference in mortality rates between these two groups (P=1.00). Conclusion: Our study showed that Aprotinin is more effective at controlling post-operative hemorrhage than Amicar. However, this did not correlate to a difference in mortality rates between patients taking these two drugs. Therefore neither Aprotinin or Amicar contributes to an increased mortality risk in patients undergoing cardiac surgery.

Supported by: U of Kentucky Division of Cardiothoracic Surgery and U of Kentucky College of Medicine
Primary Presenter / e-mail: Koul, A. / abhinav.koul@uky.edu
Mentor or Senior Author / e-mail: Ramaiah, C. / crama01@uky.edu

25	**Abstract Title:**	**Delay Discounting Predicts Differential Sensitivity to Amphetamine Reward, But not Methylphenidate Reward, in Rats**

Author(s):
J. R. Yates, Department of Psychology, U of Kentucky
M. T. Bardo, Department of Psychology, U of Kentucky

Abstract:
Impulsivity has been linked to increased drug abuse vulnerability in adolescents and young adults. Individuals who are impulsive are more likely to use and abuse drugs compared to individuals who are self-controlled. The present preclinical study was designed to determine if a correlation exists between impulsivity and conditioned place preference (CPP) using either amphetamine or methylphenidate. Seventy-eight Sprague Dawley rats were first trained in a delay discounting task, in which rats chose between a small, immediate reward and a larger, delayed reward. Animals that demonstrated the strongest preference for the small immediate reward were designated as impulsive. Rats were then tested for either amphetamine or methylphenidate CPP in which injections of either amphetamine (0.1, 0.5, or 1.5 mg/kg), methylphenidate (10 or 20 mg/kg), or saline were paired with one side of a CPP chamber. Following conditioning, preference scores were determined by allowing the rat free access to both end compartments, and these preference scores were correlated with the scores obtained from the delay discounting task. Rats high in impulsivity spent more time in the compartment paired with amphetamine compared to those low in impulsivity following 0.5 mg/kg amphetamine. In contrast, methylphenidate failed to produce CPP in either high or low impulsive rats; however, methylphenidate did produce hyperactivity in both groups. The results suggest that impulsivity may be related to differential sensitivity to amphetamine reward, but not methylphenidate reward, thus implicating individual differences in impulsivity on vulnerability to amphetamine abuse.

Supported by: NIH grant P50 DA05312
Primary Presenter / e-mail: Yates, J. R. / yates0615@gmail.com
Mentor or Senior Author / e-mail: Bardo, M. T. / mbardo@email.uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

26	**Abstract Title:**	**GZ-793A, a novel vesicular monoamine transporter-2 (VMAT2) inhibitor that probes multiple sites on VMAT2 as a potential treatment for methamphetamine abuse**

Author(s):
D. B. Horton, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
G. Zheng, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
A. G. Deaciuc, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
P. A. Crooks, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
L. P. Dwoskin, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky

Abstract:

A lobelane analog, GZ-793A [*R*-N-(2,3-dihydroxypropyl)-2,6-cis-di-(4-methoxy-phenethyl)piperidine hydrochloride] inhibits methamphetamine (METH)-evoked dopamine (DA) release from rat striatal slices, as well as METH self-administration in rats through an interaction with the vesicular monoamine transporter-2 (VMAT2). GZ-793A potently inhibits [^{3}H]DA uptake at VMAT2 (Ki = 0.029 μM), being >50-fold more selective for VMAT2 than for the DA transporter (Ki = 1.57 μM) and >300-fold more selective for VMAT2 than for the serotonin transporter (Ki = 9.36 μM). Similar to lobelane, GZ-793A does not interact with α4β2* or α7* nicotinic receptors (Ki < 100 μM). Despite the potent inhibition of VMAT2 function by GZ-793A, the analog did not potently inhibit [^{3}H]dihydrotetrabenazine (DTBZ) binding to VMAT2 (Ki = 8.29 μM), suggesting that it interacts with an alternative site on VMAT2 to inhibit DA uptake. Kinetic analyses of [^{3}H]DA uptake into striatal vesicles revealed that GZ-793A increased Km without altering Vmax compared to control, suggesting that GZ-793A competitively inhibits DA uptake at VMAT2. In a biphasic manner, GZ-793A releases [^{3}H]DA from preloaded vesicles, fitting a 2-site model (EC_{50},site 1 = 14.3 nM; EC_{50},site 2 = 33.0 μM). Incubation of [^{3}H]DA-preloaded vesicles with GZ-793A and 30 nM tetrabenazine (TBZ) blocked GZ-793A-evoked release at site 1, without altering evoked release at site 2. Taken together with the finding that GZ-793A has low affinity for the DTBZ binding site, these results suggest that TBZ allosterically inhibits GZ-793A-evoked release. METH also evokes [^{3}H]DA release from preloaded vesicles (EC_{50} = 6.9 μM; Emax = 87%) to increase cytosolic DA. GZ-793A (3 nM - 1 μM) decreased the Emax for METH-evoked [^{3}H]DA release from preloaded vesicles, which was not surmounted by increasing concentrations of METH, suggesting a noncompetitive interaction with the METH-evoked DA release site on VMAT2. Thus, GZ-793A interacts with several sites on VMAT2, having a low affinity for the DTBZ site, a high affinity competitive interaction with the DA substrate site, and a high affinity noncompetitive interaction at the site at which METH evokes DA release. Therefore, GZ-793A, a new prototypical METH inhibitor importantly inhibits the effects of METH on VMAT2 in a manner that cannot be surmounted by increasing concentrations of METH and represents a lead compound with a novel mechanism of action in the discovery of potential therapeutics for the treatment of METH abuse.

Supported by: NIH DA13519 NIH DA 016176

Primary Presenter / e-mail: Horton, D. B. / dbhort2@email.uky.edu
Mentor or Senior Author / e-mail: Dwoskin, L. P. / ldwoskin@email.uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

27	**Abstract Title:**	**Preclinical Evaluation of r-b3,5L/3PiDDB: an Allosteric alpha6beta2 Subtype-Selective Nicotinic Receptor Antagonist that Specifically Decreases Nicotine Self-Administration**

Author(s):
A.M. Smith, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
A.C. Meyer, Center for Drug Abuse Research Translation, Department of Psychology, U of Kentucky
M. Pivavarchyk, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
T.E. Wooters, Center for Drug Abuse Research Translation, Department of Psychology, U of Kentucky
Z. Zhang, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
G. Zheng, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
J.M. McIntosh, Departments of Psychiatry and Biology, U of Utah
P.A. Crooks, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
M.T. Bardo, Center for Drug Abuse Research Translation, Department of Psychology, U of Kentucky
L.P. Dwoskin, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky

Abstract:

Currently available smoking cessation pharmacotherapies have only limited efficacy, and relapse rates continue to be high, indicating that novel medications are needed. Previous studies found that the alpha6-containing nicotinic receptor (nAChR) antagonist N,N-dodecane-1,12-diyl-bis-3-picolinium dibromide (bPiDDB) inhibits (IC50=2 nM; Imax=76%) nicotine-evoked dopamine release from striatum and decreases nicotine self-administration in rats. The current study evaluated the preclinical pharmacology of two bPiDDB analogs, 3,5-dimethyl-1-(12-(3-methylpyridin-1-ium-1-yl)dodecyl)pyridin-1-ium (b3,5L/3PiDDB) and 1-(12-(3,5-dimethyl-5,6-dihydropyridin-1(2H)-yl)dodecyl)-5-methyl-1,2,3,4-tetrahydropyridine dihydrochloride (r-b3,5L/3PiDDB). Both b3,5L/3PiDDB (IC50=430 pM;Imax=76%) and r-b3,5L/3PiDDB (IC50=58 pM;Imax=60%) inhibited nicotine-evoked [3H]dopamine release from striatal slices with 5- and 33-fold higher potencies than that observed with bPiDDB. To determine whether b3,5L/3PiDDB and r-b3,5L/3PiDDB interact with alpha6-containing nAChRs that mediate nicotine-evoked dopamine release, striatal slices were exposed concurrently to maximally effective concentrations of either b3,5L/3PiDDB or r-b3,5L/3PiDDB and the alpha6-selective antagonist alpha-conotoxin MII (alpha-CtxMII). Co-exposure of alpha-CtxMII with either analog failed to produce greater inhibition than that observed with the analogs alone, suggesting that both analogs act at alpha6-containing nAChRs. Inhibitory effects of the analogs were determined in nicotine-sensitized rats (0.4 mg/kg nicotine for 10 days, sc), and a >1000-fold increase in potency for (IC50=0.21 pM;Imax=77%) was found, whereas no increase in potency was found for r-b3,5L3PiDDB. Mechanism of action was determined for the more drug-like analog r-b3,5L/3PiDDB. Schild analysis revealed a rightward and downward shift in the nicotine concentration response, and the regression slope was significantly different from 1.0, consistent with allosteric inhibition. Acute r-b3,5L/3PiDDB decreased nicotine self-administration; tolerance to this effect did not develop across 7 daily treatments. These results support our approach towards developing subtype-selective nAChR antagonists as therapeutic agents for smoking cessation and suggest that r-b3,5L/3PiDDB has potential as a clinical candidate for the treatment for smoking cessation.

Supported by: USPHS Grants U19 DA17548, R01 MH53631 and T32 DA016176

Primary Presenter / e-mail: Smith, A. M. / andrewsmith@uky.edu
Mentor or Senior Author / e-mail: Dwoskin, L. P. / ldwoskin@email.uky.edu

28 **Abstract Title:** **Prefrontal Cortex Glutamate: Transient Signaling and the Effects of Methylphenidate**

Author(s):
C. E. Mattinson, Center for Microelectrode Technology, Department of Anatomy and Neurobiology, U of Kentucky
J. S. Beckmann, Center for Drug Abuse Research Translation, Department of Psychology, U of Kentucky
J. A. Marusich, RTI International, Research Triangle Park, NC
F. Pomerleau, Center for Microelectrode Technology, Department of Anatomy and Neurobiology, U of Kentucky
P. Huettl, Center for Microelectrode Technology, Department of Anatomy and Neurobiology, U of Kentucky
M. T. Bardo, Center for Drug Abuse Research Translation, Department of Psychology, U of Kentucky
G. A. Gerhardt, Center for Microelectrode Technology, Department of Anatomy and Neurobiology, U of Kentucky

Abstract:
The medial prefrontal cortex (mPFC) is an area of the brain that is necessary for executive function, and is also implicated in neuropathologies including drug addiction. The mPFC both sends and receives glutamatergic input, and the projection from the mPFC to the nucleus accumbens is hypothesized to be critically involved in the rewarding properties associated with drug addiction. To measure glutamate in the mPFC, we have used our microelectrode array (MEA) technology. Our ceramic based MEAs detect glutamate on platinum recording sites through the use of the enzyme glutamate oxidase. A unique feature of the MEA is the ability to subtract the background current on sentinel sites from the glutamate current on enzyme coated sites, thus isolating a self-referenced glutamate signal that reflects in vivo concentrations. We examined the effects of methylphenidate (MPH) on glutamate levels in the cingulate cortex (Cg1), prelimbic (PrL), and infralimbic (IL) mPFC of anesthetized rats, and found decreased tonic resting levels of glutamate in the MPH treated animals in the IL compared to saline controls. In awake, freely-moving animals, we found transient releases of phasic glutamate over the circadian cycle that significantly correlated with concentrations of released glutamate. Finally, preliminary data suggests that in awake animals treated with MPH, transient releases of glutamate had increased concentrations as compared to controls. We intend to further examine the relationship between MPH treatment and glutamate signaling in rats performing an operant task. The information obtained from these studies will provide potential therapeutic targets for drug addiction treatment.

Supported by: NIH DA016176, DA017186, and AG13494
Primary Presenter / e-mail: Mattinson, C. E. / cmattinson@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@uky.edu

29 **Abstract Title:** **Phenyl Ring-Substituted Lobelane Analogs: Inhibition of [^{3}H]Dopamine Uptake at the Vesicular Monoamine Transporter-2**

Author(s):
J.R. Nickell, Department of Pharmaceutical Sciences, U of Kentucky
G. Zheng, Department of Pharmaceutical Sciences, U of Kentucky
A.G. Deaciuc, Department of Pharmaceutical Sciences, U of Kentucky
P.A. Crooks, Department of Pharmaceutical Sciences, U of Kentucky
L.P. Dwoskin, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:
Lobeline attenuates the behavioral effects of methamphetamine via inhibition of the vesicular monoamine transporter (VMAT2). To increase selectivity for VMAT2, chemically defunctionalized lobeline analogs, including lobelane, were designed to eliminate nicotinic receptor (nAChR) affinity. The current study evaluated the ability of lobelane analogs to inhibit [^{3}H]dihydrotetrabenazine (DTBZ) binding to VMAT2 and [^{3}H]dopamine (DA) uptake into isolated synaptic vesicles, and determined the mechanism of inhibition. Introduction of aromatic substituents in lobelane maintained analog affinity for the [^{3}H]DTBZ binding site on VMAT2 and inhibitory potency in the [^{3}H]DA uptake assay assessing VMAT2 function. The most potent (Ki=13-16 nM) analogs in the series included para-methoxyphenyl nor-lobelane (GZ-252B), para-methoxyphenyl lobelane (GZ-252C) and 2,4-dichlorphenyl lobelane (GZ-260C). Affinity of the analogs for the [^{3}H]DTBZ binding site did not correlate with inhibitory potency in the [^{3}H]DA uptake assay. Importantly, the N-benzylindole-, biphenyl- and indole-bearing analogs (AV-1-292C, GZ-272B and AV-1-294, respectively) inhibited VMAT2 function (Ki =73, 127 and 2130 nM, respectively), yet had little to no affinity for the [^{3}H]DTBZ binding site. These results suggest that the analogs interact at an alternate site to DTBZ on VMAT2. Kinetic analyses of [^{3}H]DA uptake revealed a competitive mechanism for GZ-252B, GZ-252C, GZ-260C and GZ-272B. Similar to methamphetamine, these analogs released [^{3}H]DA from the vesicles, but with higher potency . In contrast to methamphetamine, these analogs had higher potency (>100-fold) at VMAT2 than DAT, predicting low abuse liability. Thus, modification of the lobelane molecule affords potent, selective inhibitors of VMAT2 function and reveals two distinct pharmacological targets on VMAT2.

Supported by: The National Institutes of Health [Grants DA013519, T32 DA016176].
Primary Presenter / e-mail: Nickell, J. R. / jnick2@uky.edu
Mentor or Senior Author / e-mail: Dwoskin, L. P. / ldwoskin@email.uky.edu

30 **Abstract Title: Role of Cortical Dopamine Transporters in Reward Seeking and Inhibition**

Author(s): M.Darna, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
J.A. Marusich, Department of Psychology, U of Kentucky
M. T. Bardo, Department of Psychology, U of Kentucky
L. P. Dwoskin, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky

Abstract:
Vulnerability to drug abuse is related to the sensation seeking personality trait, which represents two component constructs that can be designated as reward seeking and inhibition. The mesocorticolimbic dopamine (DA) system has been implicated in reward seeking, whereas inhibition is subserved by both DA and serotonin (5-HT) in frontal cortical systems. The frontal cortex is subdivided functionally into the medial prefrontal cortex (mPFC), which has been implicated in both reward seeking and inhibition, and the orbitofrontal cortex (OFC), which has been implicated primarily in inhibition. Extracellular DA is dependent upon both presynaptic release and uptake processes, indicating that the DA transporter (DAT) may be an important molecular target underlying individual differences in sensation seeking. In the current study, we used an animal model to investigate the role of DAT in mPFC and OFC obtained from individual rats as a potential link between reward seeking and drug self-administration, and between inhibition and drug self-administration. Across a 60-day period, rats were tested on 6 behavioral tasks as predictor variables to evaluate individual differences in reward seeking and inhibition, followed by d-amphetamine self-administration (0.0056-0.1 mg/kg/infusion, for 33 days) as the outcome variable. Subsequently, kinetic analysis of [3H]DA uptake (DAT function) to obtain Km and Vmax was determined using synaptosomes prepared from mPFC and OFC obtained from the individual rats, and correlations with behavioral predictor variables generated. Results showed no correlation between the kinetic parameters of DAT function in mPFC and any of the behavioral predictor variables. Importantly, individual differences in Vmax for [3H]DA uptake by DAT in OFC was positively correlated with progressive ratio breakpoint for sucrose reinforcement (Pearson correlation, $r = 0.5214$, $p < 0.05$), indicating that extracellular DA in OFC is related to the level of motivation for sucrose reward (reward seeking).

Supported by: NIH grant: P50 DA05312
Primary Presenter / e-mail: Darna, M. / mahesh.darna@uky.edu
Mentor or Senior Author / e-mail: Dwoskin, L. P. / ldwoskin@uky.edu

31 **Abstract Title: Acyclic Lobelane Analogs as Novel Inhibitors of the Vesicular Monoamine Transporter-2**

Author(s): Z. Cao, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
G. Zheng, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
D. B. Horton, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
A. G. Deaciuc, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
P. A. Crooks, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky
L. P. Dwoskin, Department of Pharmaceutical Sciences, College of Pharmacy, U of Kentucky

Abstract:
Lobeline decreases methamphetamine (METH) self-administration by inhibiting the vesicular monoamine transporter-2 (VMAT2). Lobelane, a defunctionalized and saturated analog of lobeline, exhibits increased affinity and selectivity for VMAT2 over nicotinic receptors and dopamine (DA) transporters in comparison with lobeline. The goal of the current study was to determine potency and activity of several acyclic lobelane analogs at VMAT2 and their mechanism of inhibition. Acyclic lobelane analogs had Ki values of 3.3-300 nM in VMAT2 [^{3}H]DA uptake assays. Analogs with 3-4 carbons in the linkers between the phenyl ring and the N atom had the highest affinity for VMAT2. Replacing the homoamphetamine with an amphetamine moiety resulted in a 1.9-13-fold increase in affinity for VMAT2. Removing the methyl substituent on the N atom resulted in a 1.7-24-fold increase in affinity for VMAT2. Analogs with one chiral center connected to the N atom were racemic mixtures. Thus, the pure enantiomers GZ-878A and GZ-878B, GZ-880A and GZ-880B, as well as GZ-924 and GZ-925 were tested. Kinetic analyses of [^{3}H]DA uptake revealed a competitive mechanism of inhibition. GZ-924 had >100-fold higher affinity at VMAT2 than at the DA transporter, predicting low abuse liability. GZ-924 also released [^{3}H]DA from vesicles but with a much greater potency than METH. GZ-924 showed 11-fold increased affinity for VMAT2 uptake, 62-fold increased EC_{50} for vesicular [^{3}H]DA release and 10-fold decreased affinity for DA transporter function compared to its enantiomer, GZ-925. Thus, stereochemistry of acyclic lobelane analogs was critical for VMAT2 interaction. In conclusion, modification of the lobelane molecule afforded acyclic lobelane analogs which were potent, selective inhibitors of VMAT2 function.

Supported by: NIH DA13519
Primary Presenter / e-mail: Cao, Z. / zheng.cao@uky.edu
Mentor or Senior Author / e-mail: Dwoskin, L. P. / ldwoskin@email.uky.edu

32 **Abstract Title: A Culturally Sensitive Smoking Cessation Outreach Strategy for Rural Adults**

Author(s): K. Butler, College of Nursing, University of Kentucky
S. Hedgecock, College of Nursing, University of Kentucky
S. Derifield, Lawrence County Cooperative Extension, University of Kentucky
C. McGinn, Lawrence County, KY, Health Department
R. Record, College of Nursing, University of Kentucky
S. Adkins, College of Nursing, University of Kentucky
M. Rayens, College of Nursing, University of Kentucky
D. Murray, College of Agriculture, University of Kentucky
E. Hahn, College of Nursing, University of Kentucky

Abstract:
Background: This study examines acceptability, effectiveness and reach of a population-based, culturally sensitive intervention to motivate smokers in a rural, underserved county to participate in tobacco dependence treatment (TDT). The low-literacy outreach interventions were developed based on personal narratives. Methods: The study had three phases. Personal narratives from focus groups with smokers/former smokers (N=21) were analyzed to identify themes guiding the intervention including printed materials, earned/paid media, and a quilt made by local artisans. Cooperative Extension agents provided brief TDT interventions and outreach options. An RDD population-based survey evaluated reach and effectiveness. Results: A total of 6,241 tailored, culturally sensitive materials were distributed. A radio call-in show, radio and newspaper ads were placed over 3 months. The quilt was continuously displayed in various venues. A random-digit dial population-based survey (N= 287; response rate 21.2%) showed significant positive associations between intervention exposure and plans to quit smoking and plans to talk to a health care provider about quitting. Cooperative Extension agents believed the intervention was acceptable, practical, and effective. Conclusions: Culturally sensitive messaging is a data-rich strategy for the development of population-based interventions aimed at motivating rural smokers to quit. Use of personal narratives, brief TDT interventions, and inclusion of health literacy principles combines evidence-based, cost-effective strategies which can be effectively delivered by Cooperative Extension agents and local health departments. Pilot findings will guide future studies to test the effects of outreach interventions on TDT enrollment, attendance, nicotine dependence, and quit outcomes in rural populations.

Supported by: The development of the HEEL program was made possible by Senator Mitch McConnell with funds earmarked for the University of Kentucky, College of Agriculture, Lexington, KY and budgeted through the CSREES/USDA Federal Administration.

Primary Presenter / e-mail: Butler, K. M. / karen.butler@uky.edu
Mentor or Senior Author / e-mail: Hahn, E. J. / ejhahn00@email.uky.edu

33 **Abstract Title: UPforBenzos: Universal Precautions for Benzodiazepine prescribing**

Author(s): C. S. Carvalho, Department of Psychiatry, University of Kentucky

Abstract:
Introduction: Benzodiazepine dependence is relatively uncommon in the general population. It can be a problem in specific groups such as those with current or past substance use, coexisting psychiatric illness or a family history of substance use. Providers should be vigilant when prescribing them but there are no clear guidelines or standards. One strategy is the ˜universal precautions" approach used with opiates in pain treatment wherein a list of pre- or currently existing risk factors guide the practitioner. Relevance: This topic is important to scientists and practitioners alike. Providers are especially likely to prevent or detect & treat substance use in a high risk population. Methodology: Principles of the “universal precautions" approach was taken from the literature pertaining to its use with opiates in pain treatment. Additional commonsense & clinically relevant factors were added. Information was then consolidated into an easy to use checklist. Results: 19 different factors were identified and included in the checklist. The checklist can be rapidly administered. It can be included or be used separate from the medical record. Familiarity with addiction in clinical practice is helpful while using the form. It can be used by clinicians or staff and is designed for initial evaluation and prospective monitoring. Conclusion: Practitioners are expected to prescribe benzodiazepines carefully and judiciously especially in patient groups at high risk of abusing them. The literature however is not very informative on how careful prescribing can be practiced. Licensing and other monitoring boards also take the approach of advocating careful prescribing without offering clear guidelines. Primary care practitioners are the largest prescribers and the ones most in need of guidance that can be incorporated into their usually busy practices. This checklist called the Universal Precautions for Benzodiazepine prescribing (UPforBenzos) offers a solution to some of these challenges allowing safe prescribing.

Primary Presenter / e-mail: Carvalho, C. / cscarv2@uky.edu
Mentor or Senior Author / e-mail: Carvalho, C. / cscarv2@uky.edu

34 **Abstract Title: Non-medical Use of Prescription Drugs and HIV Risk Behaviors Among Homeless Men**

Author(s): P.K. Elliston, Center on Drug and Alcohol Research, U of Kentucky J. M. Webster, Department of Behavioral Science/Center on Drug and Alcohol Research, U of Kentucky
A. Cronen, Hope Center Inc, Lexington, Kentucky

Abstract:
Studies indicate that the prevalence of HIV among homeless people is between 3% - 20%. In general, the homeless have higher rates of chronic diseases than housed people, due in part to the effects of lifestyle factors such as poor nutrition and exposure to severe weather (Zerger, 2003). SAMHSA (2006) reported 13% of admissions to substance use treatment were for homeless individuals and 21% of those were opiate users. Although illicit drug use has been linked to HIV risk behavior, fewer studies have examined the emerging prescription drug problem in relation to HIV risk behaviors and none to our knowledge have looked at this relation within a homeless population. The current study examines HIV risks for a marginally homeless to homeless population. As part of a larger SAMHSA-funded project, risk assessments were completed for 1842 homeless men. Participants were divided into three groups: illicit users of prescription drugs (n=460), non prescription drug users (n=453), and nondrug users (n=929). Analyses revealed that men who reported non-medical use of prescription drugs were more likely than other drug users and nondrug users to participate in HIV risk behaviors including having unprotected sex with multiple partners (18.5% vs. 15.0%/7.3%), exchanging sex for drugs, money or shelter (5.7% vs. 4.9%/1.2%), having unprotected sex with an injection drug user (17.2% vs. 5.1%/0.8%), and participating in unprotected sex while high (46.0% vs. 25.8%/6.7%). Findings suggest that it may be important to further examine illicit drugs users who abuse prescription drugs in a homeless population.

Supported by: SAMHSA TI019763
Primary Presenter / e-mail: Elliston, P. K. / pk.elliston@uky.edu
Mentor or Senior Author / e-mail: Webster, J. M. / webster@uky.edu

35 **Abstract Title: Human Capital and Social Support: Correlates of Mental Health among Women Substance Abusers**

Author(s): S. Leukefeld, College of Social Work, U of Kentucky
M. Staton-Tindall, College of Social Work and Center on Drug and Alcohol Research, U of Kentucky

Abstract:
Human capital theory suggests that higher levels of employment can improve life circumstances and can be protective for mental health. In addition, social support has been shown to be protective for mental health. However, these factors have not been explored as protective with a vulnerable population of women through the theoretical lens of human capital theory. The purpose of this study is to examine whether human capital and social support are associated with mental health problems (i.e.: depression and anxiety) experienced by women substance abusers. Data were collected from 780 homeless, substance abusing women entering one of two programs: (1) residential substance abuse treatment, or (2) peer-driven recovery services. The women were mostly white (80.2%), never married (41.4%), and had an average age of 33.2 years. Bivariate correlation analyses indicate that part-time employment (Spearman's rho=-.10, p<.01) and higher levels of perceived social support (r=-.16, p<.001) were related to lower levels of mental health problems. Human capital factors and social support were found to be significant correlates of mental health in a multivariate logistic regression model (Chi Square=25.15,p<.001). However the study variables did not account for a large amount of overall variance in the mental health model. Future research should examine other indicators of human capital theory as a framework for understanding protective factors among homeless, substance using women.

Primary Presenter / e-mail: Leukefeld, S. / s.leukefeld@uky.edu
Mentor or Senior Author / e-mail: Staton-Tindall, M. / mstindall@uky.edu

36 **Abstract Title: An Exploration of Rural Offenders' Recidivism Risk Factors by Severity Level of Alcohol Use**

Author(s):
E. A. Wahler, College of Social Work and Center on Drug and Alcohol Research, U of Kentucky
M. Staton-Tindall, College of Social Work and Center on Drug and Alcohol Research, U of Kentucky
J. M. Webster, Center on Drug and Alcohol Research and Department of Behavioral Science, U of Kentucky
R. Freeman, College of Social Work, U of Kentucky
C. Leukefeld, Center on Drug and Alcohol Research and Department of Behavioral Science, U of Kentucky

Abstract:
Aim: Many rural offenders with a history of hazardous alcohol use may be at increased risk for recidivism due to alcohol problems, mental health symptoms, and criminal thinking and have few resources for treatment. This project explores the relationship between drinking history and recidivism risk factors, including treatment motivation, psychological functioning, social functioning, and criminal thinking in a sample of rural offenders on community supervision. Methods: Participants (N=75) completed a face-to-face interview using the AUDIT, CJ-CEST and TCU-CTS, instruments measuring alcohol use, client needs and functioning, and criminal thinking. A one-way ANOVA was conducted to examine mean scores on the CJ-CEST and TCU-CTS subscales across groups of low, moderate, and high alcohol severity. Results: ANOVA results indicated there were significant differences between alcohol severity groups on the CJ-CEST and the CTS. Participants with higher levels of alcohol severity reported significantly higher problems with psychological and social functioning, higher criminal thinking scores, and higher motivation for treatment. Conclusions: Findings suggest that rural offenders with more severe levels of alcohol use have more mental health problems, social problems, and increased criminal thinking, but are also more likely to report recognition of an alcohol problem and motivation for treatment. These preliminary findings indicate that individuals most at risk for recidivism and high-risk alcohol use might be likely to benefit from treatment if services are available. Implications will be discussed for the importance of assessing offenders' alcohol use and providing services in rural areas to reduce risk factors for criminal behavior and substance abuse.

Supported by: R21-AA017937
Primary Presenter / e-mail: Wahler, E. A. / Beth.Wahler@uky.edu
Mentor or Senior Author / e-mail: Staton-Tindall, M. / mstindall@uky.edu

37 **Abstract Title: A Comparison of Appalachians Arrested for Alcohol-impaired versus Drug-impaired Driving**

Author(s):
M.F. Dickson, Center on Drug & Alcohol Research, Department of Sociology, U of Kentucky
N.E. Wasarhaley, Center on Drug & Alcohol Research, Department of Psychology, U of Kentucky
M. Staton-Tindall, Center on Drug & Alcohol Research, College of Social Work, U of Kentucky
J.M. Webster, Center on Drug & Alcohol Research, Department of Behavioral Science, U of Kentucky

Abstract:
Although alcohol is the substance most associated with driving under the influence (DUI), research suggests that drugs other than alcohol are becoming more prevalent in cases of impaired driving. In fact, recent NSDUH estimates indicate that more than 10 million Americans reported driving after illicit drug use during the past year, including driving after the non-medical use of a prescription drug. The Appalachian region of the US has particularly high rates of prescription drug misuse, but few studies have examined drugged drivers and how they compare to alcohol-impaired drivers. As part of a project examining impaired driving in rural Appalachian Kentucky, 110 DUI offenders were recruited and interviewed about their substance use, impaired driving history, and other criminal behavior. For purposes of analysis, the sample was divided into individuals arrested for an alcohol-only DUI (n=43) and those arrested for a drug-involved DUI (n=67). Analyses found that individuals arrested for drugged driving were younger (33.4 vs. 37.7) and more likely to be female (38.8% vs. 16.3%). Drugged drivers had higher prevalence of the use of cocaine/crack, sedatives, amphetamines, methamphetamine, methadone, OxyContin and other non-prescribed opiates. In addition, individuals with a drug-involved DUI arrest were more likely to report a history of mental health treatment (43.3% vs. 37.2%) and other criminal justice involvement including incarceration (52.2% vs. 37.2%). These data suggest that individuals convicted of drugged driving may have a more complicated set of comorbidities, which have implications for the types of services and treatment this set of DUI offenders may require.

Supported by: NIAAA grant #R03AA015964.
Primary Presenter / e-mail: Dickson, M. F. / megan.dickson@uky.edu
Mentor or Senior Author / e-mail: Webster, J.M. / matt.webster@uky.edu

38	Abstract Title:	**Marijuana Self-Administration in High- and Low- Impulsive Sensation Seekers Using a Modified Progressive-Ratio Procedure**

Author(s): D. C. Lee, Departments of Psychology and Behavioral Science
J. A. Lile, Department of Behavioral Science
C. G. Robbins, Department of Behavioral Science
C. A. Martin, Department of Psychiatry
T. H. Kelly, Departments of Behavioral Science and Psychology

Abstract:
Individual differences in sensitivity to drug reinforcement have been related to sensation-seeking status. This ongoing study examines THC self-administration using a modified progressive-ratio procedure in low- and high- impulsive sensation seekers. Twenty-eight of forty young adult marijuana users scoring in the upper and lower median split of population norms on the impulsive-sensation seeking subscale of the Zuckerman-Kuhlman Personality Questionnaire have completed the 8-session study consisting of four 2-session test blocks. During the first session of each block, subjects receive 8 uniform puffs from a cigarette containing THC (0, 1.75 or 3.5%). During the second session of each block, subjects can earn up to 8 puffs from the previously sampled THC concentration. The first puff is earned by completing 50 responses, and the response requirement for each subsequent puff is doubled, such that 12,750 responses are required to earn all 8 puffs. Verbal-report, performance and cardiovascular assessments are completed before, immediately after, and hourly for 3 hours after smoking. A preliminary analysis indicates that the number of earned puffs increases as a function of THC concentration (0%: 3.8 ± 2.8; 1.75%: 5.2 ± 2.6; 3.5%: 5.8 ± 1.9), demonstrating that THC functions as a reinforcer. In addition, high sensation-seekers report greater scores on several self-reports of the reinforcing effects of THC. These preliminary results suggest that high sensation seekers are more sensitive to the reinforcing effects of THC.

Supported by: DA-05312 and RR-15592
Primary Presenter / e-mail: Lee, D. C. / dclee2@email.uky.edu
Mentor or Senior Author / e-mail: Kelly, T. H. / thkelly@uky.edu

39	Abstract Title:	**Assessment of Second Hand Smoking (SHS) Exposure of Children in KY- How Much Can We Trust the Provided History?**

Author(s): E. Ashford, Department of Anesthesiology, U of Kentucky
A. Young, Department of Anesthesiology, U of Kentucky
M. Veling, Department of ENT Surgery, U of Kentucky
A. Younes, Department of ENT Surgery, U of Kentucky
P. Breheny, Department of Biostatistics, U of Kentucky
A. Reddy, Department of Anesthesiology, U of Kentucky
D. Chau, Department of Anesthesiology, U of Kentucky

Abstract:
Background: Knowledge of children's exposure to second hand smoking (SHS) is important, as SHS is associated with unhealthy effects. The hypothesis: A caregiver's report of a child's SHS exposure is reliable and correlates positively with the child's salivary cotinine levels. Cotinine is a metabolite of nicotine that has become the biomarker of choice for tobacco exposure. Its' long half-life confers the ability to quantify long-term exposure. Procedure: After IRB approval, consenting caregivers of children 3-10 years old answered a questionnaire about the child's history of SHS exposure. Then, salivary samples for cotinine analysis were obtained. The children were grouped as no SHS, intermittent SHS and daily SHS exposure (no_ SHS, int_SHS and daily_SHS respectively). Results and Statistics: Salivary samples were adequate in 89 of 120 subjects (44 no_ SHS, 8 int_SHS and 37 daily_SHS groups). Median and ranges of cotinine levels: 0.4 (0- 14.6) -no_SHS group, 1.3 (0- 2.9) -int_SHS and 3.7 (0- 25.0) -daily_SHS. Multivariate analysis for characteristics of smoking exposure found that the only significant predictor of cotinine levels were the number of smokers around the child. Discussion: There is a positive correlation between SHS report and cotinine levels. A significant variability and overlap between groups is present. Unexpectedly high levels exist in the no_SHS group. Theories: 1) Unsuspected delayed cotinine metabolism 2) More known or unknown exposure to smoking than reported, so combined true no_SHS and positive SHS subgroups may coexist. Although no clear cotinine cut-off is evident to separate both subgroups, this raises questions about reliability in the no_SHS group.

Supported by: Children's Miracle Network
Primary Presenter / e-mail: Ashford, E. / eric.ashford@uky.edu
Mentor or Senior Author / e-mail: Chau, D. / fchau0@email.uky.edu

40 **Abstract Title:** **A codrug approach for sustained naltrexone delivery through microneedle pores**

Author(s): P. Ghosh, Department of Pharmaceutical Sciences, U of Kentucky
R. R. Pinninti, Department of Pharmaceutical Sciences, U of Kentucky
A. L. Stinchcomb, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:
Purpose: The aim of the research is to develop a chemically conjugated codrug of naltrexone, an opioid antagonist, with diclofenac, a nonspecific cyclooxygenase enzyme (COX) inhibitor, that would enhance transdermal delivery of naltrexone through microneedle (MN) pores for up to seven days from one patch. MN pores help drug molecules to bypass the most important barrier to transdermal delivery, the stratum corneum. The hypothesis is that by using a chemically conjugated codrug of diclofenac, the pore lifetime can be increased by decreasing inflammatory response, thus enhancing the sustained delivery of naltrexone. Methods: The study included physicochemical characterization and in vitro permeation of a 3-O-ester codrug of naltrexone with diclofenac. Chemical and enzymatic stability studies were conducted in 0.3 M acetate buffer, pH 5.0 at 32°C and in guinea pig plasma at 37°C, respectively. In vitro experiments were conducted using full thickness Yucatan miniature pig skin, either treated with MN or intact skin for control. Both the codrug and its hydrochloride salt form were tested to measure flux and skin concentrations. All samples were stored at 4°C/-80°C until analysis by HPLC. Results: The chemical half-life of the codrug was 4.3 days and the enzymatic half-life was 6 minutes. Steady-state naltrexone flux values of 0.42 ± 0.12 nmol/cm^2/h and 5.42 ± 1.5 nmol/cm^2/h were obtained from the codrug and its hydrochloride salt respectively. The skin concentration of the codrug and the parent compounds at each 12 h interval for 48 h showed an increase in concentration of the parent compounds over time. Conclusions: All studies showed that the codrug converted back to the parent compounds, which in the case of the plasma hydrolysis was within minutes. The in vitro diffusion data showed that naltrexone can be delivered using the codrug approach and skin concentrations of diclofenac were obtained indicating that diclofenac could keep the MN pores open. By using the codrug salt, a 13-fold increase in naltrexone flux was obtained thus indicating that optimization of codrug physicochemical properties and the formulation would improve naltrexone delivery.

Supported by: NIHR01DA13425 (Partially). Data previously presented at AAPS, 2010
Primary Presenter / e-mail: Ghosh, P. / pgh222@uky.edu
Mentor or Senior Author / e-mail: Stinchcomb, A.L. / audra.stinchcomb@uky.edu

41 **Abstract Title:** **Mitochondrial Dysfunction, Altered Homeostasis and Impaired Cell Survival Signaling Are Impaired in Pink1-Related Parkinsonism**

Author(s): R. S. Akundi, Department of Anatomy and Neurobiology, U of Kentucky
L. Zhi, Department of Anatomy and Neurobiology, U of Kentucky
Z. Huang, Department of Anatomy and Neurobiology, U of Kentucky
J. D. Pandya, Department of Anatomy and Neurobiology and SCoBIRC, U of Kentucky
W. A. Cass, Department of Anatomy and Neurobiology, U of Kentucky
P. G. Sullivan, Department of Anatomy and Neurobiology and SCoBIRC, U of Kentucky
H. Büeler, Department of Anatomy and Neurobiology, U of Kentucky

Abstract:
Mutations in PTEN-induced kinase 1 (PINK1) are linked to recessive familial Parkinson's disease (PD). In cells PINK1 and Parkin (another recessive PD gene) cooperate in the selective degradation of functionally impaired mitochondria through autophagy. To further study how the loss of PINK1 affects mitochondrial function and other PD-relevant pathways in vivo, we generated and characterized a new line of Pink1-deficient (Pink1-/-) mice. Compared to wildtype mice, purified mitochondria from the brain of Pink1-/- mice displayed enhanced Ca2+-induced permeability transition (rescued by cyclosporine A). Moreover, phosphorylated c-Jun accumulated in a subpopulation of dopaminergic neurons in young Pink1-/- mice, and Pink1-deficient mice aged 6 months and older showed reduced levels of dopamine associated with increased dopamine turnover in the striatum. In response to a peripheral inflammatory stimulus Pink1-/- mice had increased levels of select cytokines in the striatum. Quantitative transcriptional profiling showed differential striatal expression of genes that regulate innate immunity and apoptosis, mitogen-activated protein kinase signaling as well as axonal sprouting and regeneration. Pink1-/- embryonic fibroblasts displayed reduced basal and inflammatory cytokine-induced NF-kappa B signaling and were severely impaired in growth factor-dependent activation of the survival kinase Akt, which is required for the protection of dopamine neurons in various animal models of PD. Collectively, these results show multiple abnormalities in the nigrostriatal system of Pink1-/- mice and cells and imply aberrant innate immune signaling and impaired activation of cell survival pathways as novel mechanisms involved in the pathogenesis of recessive Parkinson's disease.

Supported by: National Center for Research Resources (NCRR) COBRE grant P20 RR15592 Parkinson Schweiz American Parkinson's Disease Association
Primary Presenter / e-mail: Akundi, R. S. / ravi.akundi@uky.edu
Mentor or Senior Author / e-mail: Bueler, H. / hansruedi.bueler@uky.edu

42 **Abstract Title: A GDNF related peptide - dopamine neuron stimulating peptide-5 - enhances dopamine neuron function**

Author(s):
O.M. Littrell, Department of Anatomy and Neurobiology, U of Kentucky
J.L. Fuqua, Department of Anatomy and Neurobiology, U of Kentucky
A.D. Richardson, Department of Anatomy and Neurobiology, U of Kentucky
P. Huettl, Department of Anatomy and Neurobiology, U of Kentucky
F. Pomerleau, Department of Anatomy and Neurobiology, U of Kentucky
J.E. Quintero, Department of Anatomy and Neurobiology, U of Kentucky
L.H. Bradley, Departments of Anatomy and Neurobiology and Molecular & Cellular Biochemistry, U of Kentucky
D.M. Gash, Department of Anatomy and Neurobiology, U of Kentucky
G.A. Gerhardt, Department of Anatomy and Neurobiology, U of Kentucky

Abstract:
Parkinson's disease (PD) involves the loss of dopamine (DA) neurons in the substantia nigra (SN) and a subsequent loss of DA in the striatum. We have shown that glial cell line-derived neurotrophic factor (GDNF) shows robust enhancing effects on DA neuron function in numerous experimental models and possibly in humans. Despite GDNF'ss therapeutic potential, its clinical value has been questioned likely due to its limited diffusion to target areas from its large size and chemical structure. One smaller peptide derived from GDNF, dopamine neuron stimulating peptide-5 (DNSP-5), has been postulated to exhibit biological activity similar to GDNF. We tested in vitro effects of DNSP-5 in primary dopaminergic neurons from the ventral mesencephalon of rat fetuses. Cells were treated with GDNF, DNSP-5, or vehicle and morphological features of tyrosine hydroxylase positive neurons were quantified. DNSP-5 significantly increased ($p < 0.001$) morphological complexity compared to citrate vehicle and the differentiation was comparable to GDNF. To evaluate in vivo effects, a unilateral DNSP-5 treatment (30 ug) was administered directly into the SN. Striatal microdialysis was performed 28 days after treatment to determine extracellular levels of DA and its metabolites. A single treatment significantly increased (~65%) extracellular DA levels 28 days later compared to vehicle (mean ± SEM (nM): vehicle: 26.0 ± 2.7; DNSP-5: 43.1 ± 4.2; $p < 0.01$, $n = 15$) while DA metabolites were unchanged. These studies indicate that DNSP-5 has neurotrophic activity which may be relevant to the treatment of neurodegenerative diseases like PD.

Supported by: NIH Training Grant 1T32 DA022738; NIH Training Grant 5T32AG000242-14; USPHS NS39787; DA017186; AG13494; NSF EEC-0310723; PO1-13494, P50-NSO39787, and endowed funds (DMG) NIH COBRE Pilot (P20RR20171, L.H.B.), PhRMA Foundation (L.H.B.), Columbus Foundation

Primary Presenter / e-mail: Littrell, O. M. / omlitt2@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@uky.edu

43 **Abstract Title: High-Speed Chronoamperometric Recordings of Dopamine in Rodent Models of ADHD**

Author(s):
E.M. Miller, Department of Anatomy and Neurobiology, U of Kentucky
F. Pomerleau, Department of Anatomy and Neurobiology, U of Kentucky
P. Huettl, Department of Anatomy and Neurobiology, U of Kentucky
G.A. Gerhardt, Departments of Anatomy and Neurobiology, Psychiatry and Neurology, U of Kentucky
P.E.A. Glaser, Departments of Psychiatry, Pediatrics and Anatomy and Neurobiology, U of Kentucky

Abstract:
The spontaneously hypertensive rat (SHR) has been used as a model for attention-deficit/hyperactivity disorder combined type and is derived from the Wistar Kyoto rat (WKY). The WKY/NCrl from Charles River has been behaviorally characterized as inattentive and is now considered a model of ADHD inattentive type, whereas the WKY/NHsd from Harlan is the proper control. ADHD is theorized to be caused by dopaminergic (DA) dysfunction and prior microdialysis studies have revealed conflicting results in these rodent models of ADHD, indicative of a need for a better understanding of DA dynamics. We hypothesized that the two rodent models of ADHD would have decreased evoked DA and faster uptake in brain regions implicated in ADHD. In this study, we investigated evoked DA and DA uptake in the Str and nucleus accumbens core (NAc) using chronoamperometric recordings with Nafion-coated carbon fiber electrodes in the SD/NCrl, WKY/NHsd, WKY/NCrl and SHR/NCRL ($n=6$-8). We found that evoked DA release was decreased (unpaired t-test, $p<0.05$) in the dorsal Str of the SHR compared to the WKY/NCrl. We observed faster DA uptake in the intermediate Str of the SHR compared to WKY/NHsd (one-way ANOVA, $p<0.05$) and the ventral striatum and nucleus accumbens core versus the SD (one-way ANOVA, $p<0.01$). Interestingly, the WKY/NCrl displayed faster uptake in the NAc compared to the SD (one-way ANOVA, $p<0.05$). Taken together, these findings support the notion that the SHR model of ADHD has a highly over-regulated striatal DA system. In conclusion, this study aids in our understanding of DA dysfunction in this animal model of ADHD and could potentially lead to new therapies.

Supported by: Grant MH070840

Primary Presenter / e-mail: Miller, E. M. / emmo222@uky.edu
Mentor or Senior Author / e-mail: Glaser, P. E. A. / pglas0@email.uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

44	**Abstract Title:**	**Ceramic-Based Microelectrode Arrays vs. Microdialysis Probe Measurements in the CNS of Awake Animals: It's About Time**

Author(s):

P. Huettl, Department of Anatomy & Neurobiology; Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, University of Kentucky, Lexington, KY, Quanteon, LLC, Nicholasville KY
M. L. Stephens, Department of Anatomy & Neurobiology; Center for Microelectrode Technology; Morris K. Udall Parkinson's Disease Research Center of Excellence, University of Kentucky, Lexington, KY
V. A. Davis, Department of Anatomy & Neurobiology; Center for Microelectrode Technology; Morris K. Udall Parkinson's Disease Research Center of Excellence, University of Kentucky, Lexington, KY
J. E. Quintero, Department of Anatomy & Neurobiology; Center for Microelectrode Technology; Morris K. Udall Parkinson's Disease Research Center of Excellence, University of Kentucky, Lexington, KY, Quanteon, LLC, Nicholasville KY
F. Pomerleau, Department of Anatomy & Neurobiology; Center for Microelectrode Technology; Morris K. Udall Parkinson's Disease Research Center of Excellence, University of Kentucky, Lexington, KY, Quanteon, LLC, Nicholasville KY
J. Burmeister, Quanteon, LLC, Nicholasville KY
E. R. Hascup, Douglas Mental Health University Institute, McGill University, Verdun, QC, Canada
G. A. Gerhardt, Department of Anatomy & Neurobiology; Center for Microelectrode Technology; Morris K. Udall Parkinson's Disease Research Center of Excellence, University of Kentucky, Lexington, KY, Quanteon, LLC, Nicholasville KY

Abstract:

Neurotransmitter signalling occurs on a second-by-second time or faster time scale. The precise measurement of neurotransmitter resting levels, rapid release bursts and uptake kinetics are important for increasing our understanding of neurotransmission for research and clinical applications. Our ceramic-based microelectrode arrays (MEAs) have a multichannel design with unique fabrication and specialized coatings that offer greater versatility and biocompatibility than microdialysis probes. As compared to microdialysis probes MEAs sample the extracellular space directly allowing for better analysis of synaptic overflow of neurotransmitters. In addition, implanted MEAs cause far less edema or gliosis than microdialysis probes, which allows for better estimates of neuronally-based release vs. release from other sources. The new design of our advanced, uniquely fabricated MEAs provides improved performance combined with our multi-channel, dual recording sentinel site FAST technology. Our MEAs can be repeatedly used to selectively measure tonic and phasic release of many neurochemicals including but not limited to glutamate, choline, adenosine, glucose, lactate, GABA and dopamine in the CNS of awake animals. These attributes are important for the eventual use of MEAs in a clinical setting. Using this technology studies examining the pharmacological effects on resting glutamate levels in awake rats showed that glutamate levels increased by as much as 122% with the glutamate transporter blocker TBOA or decreased glutamate release by 50% with ω-conotoxin, a calcium channel blocker. Studies looking at TTX, LY341495, LY379268 and CPG effects will also be presented in addition to analysis of phasic glutamate release events in awake rats.

Supported by: Quanteon, LLC, USPHS grants NS39787, DA017186, and AG13494; NSF grant EEC-0310723.

Primary Presenter / e-mail: Huettl, P. / peter.huettl@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@uky.edu

45 **Abstract Title: Evolution of Microelectrode Arrays for Intracerebral Simultaneous Monitoring of GABA and Glutamate**

Author(s):
D. A. Price, Department of Anatomy and Neurobiology, Morris K. Udall Parkinson's Disease Research Center of Excellence and Center for Microelectrode Technology, U of Kentucky
J. J. Burmeister, Center for Microelectrode Technology, U of Kentucky
F. Pomerleau, Department of Anatomy and Neurobiology, Morris K. Udall Parkinson's Disease Research Center of Excellence and Center for Microelectrode Technology, U of Kentucky
P. Huettl, Department of Anatomy and Neurobiology, Morris K. Udall Parkinson's Disease Research Center of Excellence and Center for Microelectrode Technology, U of Kentucky
G. A. Gerhardt, Department of Anatomy and Neurobiology, Morris K. Udall Parkinson's Disease Research Center of Excellence and Center for Microelectrode Technology, U of Kentucky

Abstract:
γ-Aminobutyric acid (GABA) and glutamate are ubiquitous neurotransmitters and are implicated in various neural processes and diseases. Because current real-time methods for measuring GABA and glutamate (e.g. microdialysis) are limited by poor spatial-temporal resolution, there is a need for the development and use of technologies for rapid, reliable and spatially resolved in vivo measures of both molecules. Here, we present progress made towards developing a neural device for the 4 Hz simultaneous detection of CNS GABA and glutamate using microelectrode array (MEA) technology coupled with amperometry. Because GABA and glutamate are non-electroactive, degradative enzymes (GABase and glutamate oxidase) are immobilized over MEA platinum recording sites to convert them to electroactive H2O2 reporter molecules that oxidize at the electrode surface. By configuring a pair of sites that responds to GABA+glutamate and another pair that is sensitive to glutamate-only, current measured on glutamate-only sites can be subtracted from GABA+glutamate sites to yield the GABA-specific signal. Before intracerebral implantation, MEAs are calibrated in vitro to equate a change in current to a change in concentration. GABA and glutamate dynamics were studied in the prefrontal cortex (PFC) and dorsal striatum of anesthetized rats. This study demonstrates for the first time a neural device that is capable of sub-second simultaneous monitoring of GABA and glutamate in the CNS and serves as a platform for adapting this technology for translational research involving intracerebral neurochemical monitoring in non-human primates and humans.

Supported by: NSF DBI 0754296, DARPA N66001-09-C-2080 and NIH T32 AG000242
Primary Presenter / e-mail: Price, D. A. / David.A.Price@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@uky.edu

46 **Abstract Title: Developing Biomarkers to Detect Traumatic Brain Injury**

Author(s):
S. Ghoshal, Department of Gerontology and Sanders-Brown Center on Aging, U of Kentucky
R. Guttmann, Department of Gerontology and Sanders-Brown Center on Aging, U of Kentucky

Abstract:
Activation of calpains, calcium-dependent cysteine proteases, in pathological conditions such as traumatic brain injury (TBI) is generally considered to be an important contributing factor to cellular dysfunction. Generally this is due to calpain involvement in pathways such apoptosis, necrosis and related cytosolic mediators of programmed cell death. In addition, calpain cleaves other substrates that are linked to loss of cellular integrity or disruption of other second messenger systems suggesting that calpain over activation can have multiple consequences. Thus, the ability to monitor the time, location and extent of calpain proteolytic activity would increase our understanding of TBI pathological progression and, by extension, improve our abilities to test therapeutic strategies to improve patient outcomes following brain injury. In the present study, we have determined the location of calpain cleavage sites within several known substrates of calpain that have been observed to be proteolyzed by calpain in TBI. Following in vitro digestion, calpain-mediated fragments were isolated and sequenced by Edman degradation to locate the precise cleavage site. Based on these sequences we have generated a series of neo-epitope antibodies to recognize the formation of the newly formed amino- or carboxy-termini that allow for the monitoring of calpain-activity. Using these neo-epitope antibodies we have been able to identify the formation of calpain-specific fragment patterns in homogenates of TBI injured mice of isoforms to NMDA receptor subunit NR2A. Additional targets including troponin I, nNOS, tau, and PKC gamma also appear to be well-suited for analysis using a neo-epitope approach. These antibodies will be useful biomarkers for progression of neurodegeneration and provide insight into the mechanisms of delayed neuronal death in which calpain activation is thought to contribute. In addition to the generation of these neo-epitope antibodies, we are also using phage display to pan serum samples from experimentally injured mice as a secondary approach to develop TBI biomarkers.

Supported by: NIH award: 5PO1NS058484
Primary Presenter / e-mail: Ghoshal, S. / sghos2@uky.edu
Mentor or Senior Author / e-mail: Guttmann, R. / rodneyg@email.uky.edu

47	**Abstract Title:**	**Chronic Methylphenidate and Atomoxetine During Adolescence on Dopamine Transporter Function in a Rodent Model of ADHD: Consequences of Long-term Treatment**

Author(s):
S. Sen, Department of Pharmaceutical Sciences, U of Kentucky
A. Deaciuc, Department of Pharmaceutical Sciences, U of Kentucky
K. M. Kantak, Department of Psychology, Boston University, Boston, MA
L. P. Dwoskin, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:
Attention deficit hyperactivity disorder (ADHD) is characterized by dysfunctional medial prefrontal cortex (mPFC), orbitofrontal cortex (OFC) and striatum. ADHD treatment with methylphenidate (MPH) or atomoxetine (ATO) typically continues through adolescence, when mPFC and OFC are vulnerable to pharmacological insult. ADHD and cocaine addiction are often comorbid; however, the effect of MPH or ATO during adolescence on cocaine addiction in ADHD patients is unclear. Our previous studies showed that MPH treatment during adolescence increased cocaine self-administration during adulthood in spontaneously hypertensive rats (SHR), an animal model of ADHD, when compared to its genetic control, Wistar-Kyoto (WKY), and an outbred control strain, Wistar (WIS) rats. We hypothesize that MPH-induced increase in dopamine transporter (DAT) function leads to increased self-administration of cocaine in SHR relative to WKY and WIS. We predict that ATO will not increase DAT function or increase cocaine self-administration. [^{3}H]Dopamine (DA) uptake conducted in mPFC, OFC and striatal synaptosomes revealed no differences in Vmax of DAT between the strains. In SHR, MPH increased Vmax in mPFC, but not OFC or striatum, relative to control. MPH decreased Vmax in WKY OFC compared to control. In contrast, in SHR and WIS, ATO decreased Vmax in OFC relative to WKY. In SHR, ATO decreased Vmax in striatum compared to control. In conclusion, MPH-mediated increases in DAT function in the SHR mPFC may underlie the increased cocaine self-administration observed previously. ATO does not alter DAT function in mPFC and thus may not increase cocaine self-administration (experiments in progress).

Supported by: NIH grant R01 DA011716
Primary Presenter / e-mail: Sen, S. / sucharita.sen@uky.edu
Mentor or Senior Author / e-mail: Dwoskin, L. P. / ldwoskin@email.uky.edu

48	**Abstract Title:**	**Analysis of Rapid Glutamate Transients in the Hippocampus Reveals That Pre-Status Epilepticus Basal Glutamate Levels Predicts Severity of Status Epilepticus in Aged Animals.**

Author(s):
F. Pomerleau, Anatomy & Neurobiology, Center for Microelectrode Technology, U. of Kentucky
M. L. Stephens, Anatomy & Neurobiology, Center for Microelectrode Technology, U. of Kentucky
P. Huettl, Anatomy & Neurobiology, Center for Microelectrode Technology, U. of Kentucky
G. A. Gerhardt, Anatomy and Neurobiology, Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, U. of Kentucky

Abstract:
The excitatory neurotransmitter L-glutamate is responsible for signaling in the hippocampus trisynaptic pathway (DG, CA3 and CA1) and it has been widely suggested that dysregulation of excitatory neurotransmission is involved in epileptic seizures, which is more prevalent in the aged brain. Recordings were performed in awake rats using enzyme-based microelectrode arrays (MEAs) configured for self-referencing recordings. The self-referencing ability of our MEAs allows us to accurately measure basal levels by the subtraction of interferents and background noise. The temporal resolution of our MEAs (~ 500 ms) allows us to measure rapid glutamate bursting events that occur over 2-4 seconds. Young (3-6 months) and aged (24 months) male F344 rats were implanted with modified MEAs. A guide cannula was attached to allow for intrahippocampal injections of 4-aminopyridine (4-AP), a K+ channel blocker, to induce status epilepticus (SE). Recordings showed that basal glutamate in all hippocampal subregions of aged rats were higher than young rats (aged vs. young, DG: 17.3 ± 12.6 μM vs. 7.9 ± 1.4 μM; CA3: 22.2 ± 7.1 μM vs. 11.7 ± 2.9 μM; CA1: 10.7 ± 4.3 μM vs. 6.2 ± 1.0 μM). Aged animals experienced longer SE than younger animals (105 ± 15 min. vs. 55 ± 10 min). Furthermore, aged animals with higher pre-status tonic (basal) glutamate levels experienced longer SE. These data are the first studies to demonstrate phasic glutamate release during SE and a potential relationship between resting glutamate levels and SE severity in aging.

Supported by: USPHS AG00242, DA017186, NS39787, AG013494, NSF EEC-0310723
Primary Presenter / e-mail: Pomerleau, F. / francois.pomerleau@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@uky.edu

49	**Abstract Title:**	**In Vivo Studies of the Effects of Kindling on Rapid, Spontaneous Glutamate Release in Sub-Regions of the Rat Hippocampus**

Author(s):
V.A. Davis, Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, Anatomy & Neurobiology, U of Kentucky
M.E. Deel, Center for Microelectrode Technology, Anatomy & Neurobiology, U of Kentucky
M.L. Stephens, Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, Anatomy & Neurobiology, U of Kentucky
R.M. Alcala, Neurology, U of Kentucky
J.E. Quintero, Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, Anatomy & Neurobiology, U of Kentucky
F. Pomerleau, Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, Anatomy & Neurobiology, U of Kentucky
P. Huettl, Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, Anatomy & Neurobiology, U of Kentucky
J.T. Slevin, Neurology, U of Kentucky
G.A. Gerhardt, Center for Microelectrode Technology, Morris K. Udall Parkinson's Disease Research Center of Excellence, Anatomy & Neurobiology, U of Kentucky

Abstract:
Aberrant regulation of glutamate has been strongly implicated in epilepsy, a chronic neurological condition affecting about 2 million Americans. In these studies we examined glutamate neurotransmission in an animal model of epilepsy to determine if kindling caused long-term changes in hippocampal glutamate signaling. We used enzyme coated microelectrode arrays (MEAs) coupled to amperometry to directly study rapid glutamate neurotransmission in vivo. The small size of each MEA recording site (15 x 333 µm) allows targeting of discrete hippocampal sub-regions affected by seizures. Male Sprague Dawley rats were kindled by implantation of a small Teflon-coated, stainless steel bipolar twisted wire. Electrical stimuli were applied once/day until seizures occurred during two consecutive daily stimulations. Control animals were implanted with wires, but no electrical current was applied. Four weeks later, we used glutamate sensitive MEAs to examine glutamate neurotransmission in the DG, CA3 and CA1 sub-regions of the hippocampus in isoflurane anesthetized rats. In both control and kindled animals, spontaneous, rapid, transient glutamate release (transients) was observed. The number of transients and the interval between them was not significantly different between treatment groups, however the amplitude of transients in the DG of kindled animals (3.01 ± 0.96 µM, N=12) was significantly increased versus control animals (0.77 ± 0.16 µM, N=13. $p = 0.0255$). Conversely, in CA3, the amplitude of transients in kindled animals (0.46 ± 0.11 µM, N=11) is significantly decreased compared to control animals (3.02 ± 1.06 µM, N=12. $p = 0.0316$). These findings suggest that the perforant pathway is involved in glutamate modulation in a kindled animal model of epilepsy. Further understanding of the role of the perforant pathway in the regulation of aberrant glutamate could lead to potential epilepsy treatments.

Supported by: VA Merit Grant (Dr. Slevin), DAO17186 and NS39787
Primary Presenter / e-mail: Davis, V. A. / verda@uky.edu
Mentor or Senior Author / e-mail: Gerhardt, G. A. / gregg@uky.edu

50 **Abstract Title:** **Characterization of the Intrinsic Molecular and Protective Properties of the Synthetic Dopamine Neuron Stimulating Peptides**

Author(s):
K.A. Kelps, Department of Anatomy & Neurobiology, U of Kentucky
J. Turchan-Cholewo, Department of Anatomy & Neurobiology, U of Kentucky
T.L. Taylor, Department of Anatomy & Neurobiology, U of Kentucky
D.M. Gash, Department of Anatomy & Neurobiology, U of Kentucky
G.A. Gerhardt, Department of Anatomy & Neurobiology, U of Kentucky
L.H. Bradley, Departments of Anatomy & Neurobiology and Molecular & Cellular Biochemistry, U of Kentucky

Abstract:
Because of its endogenous role in promoting the growth and survival of dopamine-producing neurons lost in Parkinson's disease (PD), glial cell line-derived neurotrophic factor (GDNF) has generated interest for the treatment of PD. However, GDNF has not advanced beyond clinical trials due to challenges associated with the direct delivery of large proteins to the brain. Recently, a small 11-amino acid, amidated peptide, dopamine neuron stimulating peptide-11 (DNSP-11), showed neurotrophic-like properties in primary dopaminergic neurons and parkinsonian rat models. This offers the potential for much smaller neurotrophic molecules that can be delivered and modified easily for therapeutic use. Here we evaluate the molecular and cellular protection properties of three amidated-peptides, a 5-mer (DNSP-5), 11-mer (DNSP-11), and a 17-mer (DNSP-17), hypothesized to be endoproteolytically processed from the pro- (DNSP-5, DNSP-11) and mature (DNSP-17) GDNF protein. Far-UV circular dichroism spectra show that the DNSPs are soluble and act independently in vitro. Reverse phase HPLC and mass spectrometry analysis show that the three peptides are stable for up to one month at a variety of storage and experimental conditions. To gain insight into the their biodistribution properties in the brain, we used affinity chromatography to show that DNSP-17 binds heparin equally as tight as GDNF, whereas DNSP-5 and DNSP-11 do not bind heparin, which should facilitate their delivery in vivo. Finally, we present data showing that DNSP-11 provides dose-dependent protection of HEK-293 cells from staurosporine and 3-nitropropionate (3-NP) cytotoxicity, thereby supporting broad mitochondrial-protective properties of these peptides.

Supported by: Training research fellowships from NIDA (T32 DA022738, K.A.K.) and NIA (T32 AG000242, J. T.-C.). This work was also supported by University of Kentucky College of Medicine Start-up Funds (L.H.B.), NIH COBRE Pilot (P20RR20171, L.H.B.), PhRMA Foundation (L. H.B.), NINDS (NS039787, G.A.G., D.M.G., L.H.B).

Primary Presenter / e-mail: Kelps, K. A. / kakelp2@uky.edu
Mentor or Senior Author / e-mail: Bradley, L. H. / lhbrad2@uky.edu

51 **Abstract Title:** **Neuroticism and Introversion Modulate Sensorimotor Brain Responses During Sentence Reading**

Author(s):
M. Dietrich, Department of Rehabilitation Sciences, U of Kentucky
R. D. Andreatta, Department of Rehabilitation Sciences, U of Kentucky
Y. Jiang, Department of Behavioral Science, U of Kentucky
A. Joshi, Department of Rehabilitation Sciences, U of Kentucky
J. C. Stemple, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
The purpose of this study was to investigate whether central brain activity related to speech production is correlated with limbic activity as a function of the personality factors of neuroticism and introversion. Twelve vocally healthy adults (22-57 years) participated in a functional magnetic resonance imaging (fMRI) study using an event-related sparse sampling design to acquire brain activation data during an overt sentence production task (whispered or voiced). Participants completed the Multidimensional Personality Questionnaire-Brief Form to form subgroups based on the factors of neuroticism and extraversion (both high vs. low). The outcome measure was the blood oxygenation level dependent signal change in prefrontal, limbic, subcortical, and primary somatosensory and motor cortices. Elevated limbic and motor cortical activations were found among participants who scored above the group median on neuroticism and introversion. Somatosensory cortical activation was significantly correlated with neuroticism, while motor cortical responses were significantly correlated with introversion only. Activation of the anterior cingulate cortex, and periaqueductal gray areas were found during the speech tasks. These limbic activations are of particular interest given that these same areas are functional during vocalization behaviors in the primate, a mammal whose entire repertoire of vocalization behaviors is driven by the limbic system. This study provides early evidence of personality-related limbic system influence on the central control of voice production. It is hypothesized that introversion and neuroticism may modulate the motor cortical control of human voice production in ways that could lead to significant vocal dysfunction. Pilot data from 10 participants who underwent the same fMRI protocol but with an additional stress reactivity component will be presented to further illustrate the influences of personality differences in the central control of voice.

Supported by: Seed grant from Office of Research, UK College of Health Sciences, pilot funding from UK Center for Clinical and Translational Science and UK Magnetic Resonance Imaging and Spectroscopy Center

Primary Presenter / e-mail: Dietrich, M. / maria.dietrich@uky.edu
Mentor or Senior Author / e-mail: Stemple, J. C. / jcstem2@email.uky.edu

52	**Abstract Title:**	**The C-RAT: A Comprehensive Risk Assessment Tool for Use before Prescribing Psychotropics**

Author(s): C. S. Carvalho, Department of Psychiatry, University of Kentucky
C. Jayaraman, Department of Psychiatry, University of Kentucky

Abstract:

Background: Completed suicide and suicide attempts are seen with significant frequency in patients with psychiatric illness. Among the many known risk factors is the recent initiation of a psychotropic medication especially antidepressants. These and other psychotropics have warnings related to suicide risk in their package insert. This requires practitioners to thoroughly evaluate suicide and violence risk before and during treatment with these medications. Completing this risk assessment in a comprehensive and time efficient manner can be challenging for many busy practitioners. Described below is an evaluation tool that helps identify risk factors and overall risk quickly. It is useful from a clinical and medicolegal standpoint. Methods: Through a literature review all known risk factors for suicide and violence were identified. Also considered were aspects of the psychiatric interview and mental status exam typically used by clinicians to determine risk with an emphasis on objective findings. Attention was also paid to information from collateral sources along with overall course of the patient's illness till the time of medication initiation. Results: Over 60 different risk and protective factors were identified. They are organized into a one- page format for quick and easy use. In addition to identifying risk factors the C-RAT also serves as an educational tool for trainees. It also indicates that the provider thoroughly assessed risk and documented these findings. Conclusions: This tool differs from existing risk assessment scales on many levels. There are plans to further study its efficacy in clinical practice.

Primary Presenter / e-mail: Jayaraman, C. / cch224@uky.edu
Mentor or Senior Author / e-mail: Carvalho, C. / cscarv2@uky.edu

53	**Abstract Title:**	**See one, do one, teach one: Educating residents on risk assessment using a comprehensive, practical & user-friendly tool**

Author(s): C. S. Carvalho, Department of Psychiatry, University of Kentucky
M. Nair, Department of Psychiatry, University of Kentucky

Abstract:

Psychiatric residents are required to learn and practice doing risk assessments in multiple settings over the course of their training. These typically determine a patient's risk of harm to self or others and allow residents and clinicians to appropriately plan treatment with a focus on strategies that decrease risk in the short term. Residents are also expected to rely on their ability to carry out a thorough psychiatric evaluation that accurately captures subjectively reported symptoms and matching objective signs. These skills vary with year of training, the time of day, patient traffic during a particular shift, resident fatigue and the presence of attending support. Teaching risk assessment to residents in a way that will allow them to carry out this task accurately and efficiently in a variety of clinical settings can be additionally challenging. Currently available tools to assess risk measure the severity of suicidal intent, and the intensity of depression, anxiety and hopelessness. Their limitations include high false positive rates, reliance on patient participation, using statistically important but not clinically relevant items, adding to the evaluation time, making documentation more cumbersome and cannot be used to foster discussion and learning simultaneous with the provision of patient care. The tool described here combines demographic and clinical facts into a single easy-to-use risk assessment method in virtually any setting. It is designed to have more clinical and teaching value than as a precise measure for use in research. Its advantages include: 1) being a learning tool that teaches the user to do a thorough risk assessment based psychiatric evaluation, 2) doesn't take extra time, 3) allows teaching and discussion by residents or faculty, 4) can be used by any type of clinician, 5) uses demographic / statistical and commonsense clinical items that need to be identified during a risk assessment, and 6) if entered into the medical record, have medicolegal value. Clinically it allows the user to thoughtfully assess risk so that ways in which it can be contained or managed are determined next based on whether the patient is admitted, discharged or expected to return for follow up.

Primary Presenter / e-mail: Nair, M. / manishnair@uky.edu
Mentor or Senior Author / e-mail: Carvalho, C. / cscarv2@uky.edu

54 **Abstract Title:** **Evert-related Potentials as Biomarkers for Early Mild Cognitive Impairment Detection**

Author(s): L. Broster, Department of Behavioral Science, MD/PhD Program, U of Kentucky
J. Li, Chinese Academy of Sciences, Institute of Psychology, Beijing, China
C. Smith, Department of Neurology, Sanders-Brown Center on Aging, and Magnetic Resonance Imaging and Spectroscopy Center, U of Kentucky
G. Jicha, Department of Neurology, Sanders-Brown Center on Aging, and Magnetic Resonance Imaging and Spectroscopy Center, U of Kentucky
Yang Jiang, Department of Behavioral Science, U of Kentucky

Abstract:
Background: Early detection of mild cognitive impairment (MCI) is an important clinical research goal. Because current gold-standard diagnostic methods are very expensive, finding accurate, inexpensive diagnostic alternatives is indicated. Objectives and Methods: To determine whether event-related potentials (ERP) associated with a working memory (WM) paradigm might diagnose preclinical Alzheimer's disease (AD), we analyzed behavioral and ERP results of a combined WM/repetition task administered to 46 subjects (18 normal, 17 MCI, 11 AD) and collected ERP data. Each subject memorized an image at the beginning of each trial and then determined whether each of 5 serially presented objects matched that image ("match/non-match"). In each trial both the image and one non-match image were presented 2-3 times. Subjects' reaction times and accuracy were compared across repetition (1st, 2nd, or 3rd image presentation) and match/non-match status for normal, MCI, and AD groups. Results: Behaviorally, normal and MCI patients performed similarly; AD patients performed worse. Within-trial repetition effects demonstrated that implicit memory influenced performance; this effect was greatest for AD patients. MCI and AD group ERP results were similar to one another and distinct from control patients'. Conclusions: 1) Behavioral results showed that simple repetition even within 30 seconds of a memory trial improved early AD patients' memory performance. This provides an empirical basis for neurocognitive AD intervention. 2) MCI patients performed like control patients, but ERP responses resembled AD patients'. ERP shows promise as a relatively inexpensive future MCI biomarker.

Supported by: Department of Energy award: DE-AC05-OR22725 and NIH award: AG00986
Primary Presenter / e-mail: Broster, L. / lukebroster@gmail.com
Mentor or Senior Author / e-mail: Jiang, Y. / yjiang@uky.edu

55 **Abstract Title:** **Affect and Cognition Related Brain Responses During a Non-Emotional Memory Task in Older Patients with Cognitive Impairment**

Author(s): S. Wing, Department of Behavioral Science- College of Medicine and 2nd Year Medical Student, U of Kentucky
R. Gu, Department of Behavioral Science- College of Medicine, U of Kentucky, and Institute of Learning and Cognition, Beijing Normal Univ., Beijing, China
G. Jicha, Department of Neurology and Sanders-Brown Center on Aging, U of Kentucky
Y. Jiang, Department of Behavioral Science- College of Medicine, Sanders-Brown Center on Aging, and Magnetic Resonance Imaging (MRI) and Spectroscopy Center, U of Kentucky

Abstract:
Recent research has demonstrated that the left and right amygdalae (key brain structures for emotion) are differentially associated with successful or failed emotional memory retrievals respectively (Smith, et al. 2005). Using functional MRI, we examined brain responses of 41 older adults recruited from UK-ADC, focusing on affect and cognitive processing pathways during a working memory task without emotional content. Thirty of the participants were cognitively normal, and 11 were diagnosed with Mild Cognitive Impairment (MCI) at the time of the experiment. We found significant differences in amygdala involvement between normal and MCI groups. 91% of MCI subjects showed right amygdala activation during working memory retrieval, likely indicating frustration with the task. In contrast, only 37% of normal older adults showed right amygdala activity. Smaller group differences were found in left amygdala activation (MCI: 55%; normal: 40%). Anterior Cingulate Cortex (ACC), an executive control region for cognitive and affective processes, also evoked enhanced responses among MCIs (MCI: 100%; normal: 76.7%). We further examined individual differences within the normal group. The left amygdala activation group, compared to the non-activated group, evoked stronger fMRI responses in the right medial frontal cortex and right inferior frontal cortex when matching targets of working memory. The right amygdala subjects showed stronger activation in ACC when identifying non-match objects, perhaps due to compensatory effort. These results have important implications for understanding the impact of emotional processing on cognitive performance among preclinical Alzheimer's patients.

Supported by: NIH AG00986 and P50 AG05144-21
Primary Presenter / e-mail: Wing, S. / sarahwing@uky.edu
Mentor or Senior Author / e-mail: Jiang, Y. / yjiang@uky.edu

56 **Abstract Title:** **Increased Cortical Capillary Density in Alzheimer's Disease is Mediated by Frontal Lobe Neurofibrillary Degeneration: The Missing Link Between Degenerative and Cerebrovascular Brain Disease**

Author(s): H.R. Sweat, University of Kentucky College of Medicine
G.A Jicha, University of Kentucky Alzheimer's Disease Center and the Sanders-Brown Center on Aging, University of Kentucky College of Medicine

Abstract:
Background: Increases in cortical capillary densities have been described in AD compared to control cases. Pathological characterization of such changes and their relationship to the hallmark amyloid plaques (NP) and neurofibrillary tangles (NFT) seen in AD has not been performed. Understanding the pathological basis for such microvascular alterations may provide important clues to the relationship between cerebrovascular disease and AD. Methods: Stereologic quantitation of brain capillary length-density was performed on Alzheimer's disease (all cases met NIA-Reagan criteria for high-likelihood of AD in the absence of other significant pathological features including cerebrovascular disease, n=10) vs. normal control (all cases met NIA-Reagan criteria for low-likelihood of AD, n=10) neocortical sections including frontal, temporal, parietal, and occipital regions. Capillary length density was correlated with quantitative neuropathological burden of NP and NFT in each discrete neocortical region. Results: Capillary length-density was greater in AD compared to control cases for all areas studied, although these differences reached statistical significance only in frontal neocortex (Brodman's area 9; $p<0.03$, Students t-Test) in the small sample studied. Frontal lobe capillary length-density was strongly associated with NFT burden ($p<0.0005$, Student's t-Test), less so with NP burden ($p<0.05$), and not at all with diffuse senile plaque burden. NFT burden was significantly higher in temporal and parietal compared to frontal and occipital regions in the cases sampled. Discussion: This study represents the first in-depth, quantitative assessment of neocortical microvascular alterations in AD subjects that lacked detectable pathological evidence for cerebrovascular disease. The findings clearly demonstrate microvascular alterations in frontal neocortex that are associated with neurofibrillary degeneration. While atrophy as a result of the degenerative process could be postulated as responsible, a higher NFT burden in temporal and parietal regions argues strongly against this possibility. Further studies investigating the changes that may underlie aberrant microvascular alterations in the frontal neocortex of AD subjects are clearly warranted.

Supported by: Professional Student Mentored Research Fellowship, UK CCTS
Primary Presenter / e-mail: Sweat, H. R. / haylea.sweat@uky.edu
Mentor or Senior Author / e-mail: Jicha, G. A. / gajich2@uky.edu

57 **Abstract Title:** **Long-Term High Fat Diet Halts Follicular Development in Mice**

Author(s): P. P. Lin, College of Health Sciences, U of Kentucky
C. J. Ko, College of Health Sciences, U of Kentucky

Abstract:
Polycystic ovarian syndrome (PCOS) is the most prevalent endocrine disorder in women of childbearing age, 70% of the PCOS patients being obese or carrying metabolic disorders. The hallmark of PCOS, however, is the formation of multiple cysts in the ovary, which results from the arrest of follicular development at early antral stage. As the developing follicles are the subjects of the endocrine regulation by metabolic hormones such as insulin and IGFs as well as the sites of steroid production (andorgens, estrogens and progesterones) that affects metabolism, changes in follicular development and metabolic milieu must be mutually influential. We therefore hypothesized that arrest of follicular development and metabolic disorders are mutually causal contributing to the vicious cycle in the PCOS patients. To test whether arrest of follicular development causes or worsens a metabolic disorder, we used C57BL/6J mice that are deficient of Esr1 gene specifically in the theca cells (Esr1flox/flox Cyp17iCre, or thEsr1KO). The female thEsr1KO mice became hyperandrogenic as early as at the age of 8 weeks, while displaying a normal range of follicular development. At the age of 22 weeks, however, the mice displayed significantly lower fertility (10.0%, n=10) than wild type (WT) control (90.9%, n=11) and their follicular development halted at early antral stages. The metabolic phenotypes of these thEsr1KO mice were examined by measuring body weight, blood pressure, body fat composition, glucose tolerance, insulin resistance, and metabolic efficiency, and the resulting data were compared with those of age-matching WT mice. There was no significant difference in all of indexes measured except that thEsr1KO mice were less tolerant to glucose than the WT control mice. To test whether metabolic disorder causes the arrest of follicular development, we induced metabolic defects by feeding 2-month old WT C57BL/6J female mice with high fat diet (60% fat calories). Control mice were fed with a regular (18% fat calories). Upon 8 weeks of high fat diet, they became obese and intolerant to glucose, but no sign of defect in follicular development was seen as they showed a normal range of fertility. However, upon 22 weeks of high fat diet, this group of mice showed dramatically lower fertility (5.9%, n=16) than regular diet mice (61.5%, n=13). Histological examination revealed that the ovaries of the infertile mice of the high fat diet group did not have any corpus luteum, an evidence of absence of ovulation, but had multiple cystic follicles and early antral stage follicles, indicating an arrest of follicular development at the antral stage. Taken together, this study demonstrates that metabolic disorders give greater impact on ovarian follicular development than a defect in follicular development does on body metabolism.

Supported by: COBRE grants from NIH NCRR: P20 RR15592 and University of Kentucky CHS Research Funds
Primary Presenter / e-mail: Lin, P. P. / pochinglin@uky.edu
Mentor or Senior Author / e-mail: Ko, C. J. / cko2@uky.edu

58 **Abstract Title: Glucose Intolerance Is Independent of Obesity in a Type 2 Diabetes Mouse Model, TALLYHO**

Author(s):
T.P. Stewart, Department of Pharmacology, Physiology and Toxicology Joan C. Edwards School of Medicine, Marshall U
C.N. Bowden, Department of Pharmacology, Physiology and Toxicology Joan C. Edwards School of Medicine, Marshall U
X. Mao, Department of Pharmacology, Physiology and Toxicology Joan C. Edwards School of Medicine, Marshall U
J.H. Kim, Department of Pharmacology, Physiology and Toxicology Joan C. Edwards School of Medicine, Marshall U

Abstract:
Type 2 diabetes (T2D) is the most common form of human diabetes, accounting for over 90% of diagnosed patients and often coexists with obesity. It is well-recognized that T2D is acquired by a combination of insulin resistance in the target tissues and failure of insulin secretion from pancreatic beta-cells. Obesity is known to be a prominent cause of insulin resistance, but only 25-30% of obese individuals progress to T2D. TALLYHO/JngJ (TH) mice are an inbred polygenic model for T2D characterized by obesity, hyperlipidemia, hyperinsulinemia, impaired glucose uptake and tolerance, and hyperglycemia. Our previous study implicated that obesity and insulin resistance are an inherent part of the TH phenotype, and glucose intolerance is evident preceding progression to overt diabetes in TH mice. In this study, we tested whether the obesity is necessary for the impaired glucose tolerance in TH mice. At 10 weeks of age, male TH mice were randomly divided into 2 groups, a control group and calorie restriction group. The control animals were maintained on ad libitum diet, while the animals in the calorie restriction group were fed a 30% energy-restricted diet compared with the ad libitum fed group for 8 weeks. The TH mice in the calorie-restricted diets exhibited a significant loss of body weight during the study. At the end of the study, this weight loss, however, was not associated with ameliorating glucose intolerance in TH mice. We conclude that obesity alone may not be sufficient to cause diabetes in TH mice.

Supported by: Institutional start-up funding from Marshall University
Primary Presenter / e-mail: Kim, J. H. / kimj@marshall.edu
Mentor or Senior Author / e-mail: Kim, J. H. / kimj@marshall.edu

59 **Abstract Title: A Novel, Nano-Scale Device to Increase Metabolism via Mitochondrial Uncoupling**

Author(s):
J.D. Pandya, Spinal Cord and Brain Injury Research Center, University of Kentucky
R.D. Readnower, Spinal Cord and Brain Injury Research Center, University of Kentucky
P.G. Sullivan, Spinal Cord and Brain Injury Research Center, University of Kentucky

Abstract:
Obesity is recognized as a national and global epidemic, as approximately 65% of adults in the United States are classified as overweight or obese as defined by body mass index. Obesity is now only second to smoking as the cause of premature death in the United States. In the 1930s it was recognized that increasing the body's basal metabolism using mitochondrial uncouplers, directly resulted in steady and rapid weight loss. During this period the mitochondrial uncoupler 2,4-dinitophenol (2,4-DNP) was sold over the counter as a weight-loss supplement. It is the only compound to date that has been shown to be 100% effective for weight-loss; however it was eventually pulled from the shelves by the FDA as people were routinely overdosing on the compound in an effort to increase their rate of weight loss. The goal of the present study was to test the hypothesis that nanotubes can be designed to act as self-rectifying proton channels in mitochondria to safely increase basal metabolism. Results from studies in isolated liver and brain mitochondria demonstrate that altering the inner diameter of nanotubes results in changes in proton conductance and that the nanotubes can be built to self-rectify at specific membrane potentials. Further studies in adult rats (n = 6-8/group), obese canines (n = 7-9/group) and a model of diet-induced obesity in mice (n = 6/group) demonstrated no overt pathology or toxicity associated with administration of the nanotubes. Furthermore, significant body weight loss was measured that ranged from 4-8 % per week in all three species. Together these results demonstrate that nanotubes can be designed that act as self-rectifying proton channels to decrease mitochondrial membrane potential, uncouple mitochondrial oxidative phosphorylation and increase metabolism resulting in significant body weight loss.

Supported by: NIH awards: R01 NS48191, R01 NS062993 (P.G.S.) and funding from the Kentucky Spinal Cord and Head Injury Research Trust
Primary Presenter / e-mail: Readnower, R. / rdread2@uky.edu
Mentor or Senior Author / e-mail: Sullivan, P. G. / patsullivan@uky.edu

60 **Abstract Title:** **Maternal Exercise During Pregnancy Improves Glucose Disposal in Mice Offspring**

Author(s):
L.G. Carter, Graduate Center for Nutritional Sciences, U of Kentucky
C.M. Tobia, Graduate Center for Nutritional Sciences, U of Kentucky
S.Y. N. Tenlep, Graduate Center for Nutritional Sciences, U of Kentucky
P. Shridas, Department of Internal Medicine, U of Kentucky Medical Center
M.L. Garcia-Cazarin, Department of Physiology, College of Medicine, U of Kentucky
G. Wolff, Department of Physiology, College of Medicine, U of Kentucky
K.A. Esser, Department of Physiology, College of Medicine, U of Kentucky
K.J. Pearson, Graduate Center for Nutritional Sciences, U of Kentucky

Abstract:
Although exercise is widely recognized as an important part of a healthy lifestyle and is known to improve cardiovascular and metabolic health, seemingly few people have time or motivation for physical activity. If exercise during pregnancy could not only protect individuals against disease, but also provide lifelong health benefits to their developing child, there should be more incentive to exercise. We hypothesize that maternal exercise during pregnancy will improve glucose regulation in offspring by increasing offspring insulin sensitivity. To study this, female ICR mice were separated into sedentary or exercise cohorts with the exercise cohort having voluntary access to a running wheel during pregnancy and nursing. Offspring were weaned and analyses were performed on the mature offspring that did not have access to running wheels during any portion of their adult lives. To evaluate glucose regulation, glucose tolerance tests were performed in male and female offspring (n = 18 - 20 per group per sex). To evaluate insulin sensitivity, insulin tolerance tests as well as ex vivo analysis of 2-deoxyglucose uptake in muscle and adipose were performed in female offspring and their tissues, respectively. Maternal exercise was found to significantly improve glucose disposal in male and female offspring ($p < 0.05$). Insulin sensitivity was also increased in offspring born to exercised dams compared to those from sedentary dams ($p < 0.05$). This data suggests that short term maternal exercise improves glucose regulation in offspring by increasing insulin sensitivity. If these findings are consistent in humans, maternal exercise could be an excellent intervention to target adulthood cardiovascular disease and diabetes.

Supported by: NIH award: R01 DK090460 to Kevin J. Pearson
Primary Presenter / e-mail: Carter, L. / lindsaygcarter@uky.edu
Mentor or Senior Author / e-mail: Pearson, K. / kevin.pearson@uky.edu

61 **Abstract Title:** **Diet-induced Obesity Decreases Striatal DopamineTransporter Function, Striatal D2 Receptor Density and Increases Motivation for High-and Low-Fat Food Reward.**

Author(s):
V. Narayanaswami, Department of Pharmaceutical Sciences, U of Kentucky
A.G. Deaciuc, Department of Pharmaceutical Sciences, U of Kentucky
L.A. Cassis, Graduate Center for Nutritional Sciences, U of Kentucky
M.T. Bardo, Department of Psychology, U of Kentucky
L.P. Dwoskin, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:
Obesity and drug abuse are hypothesized to share common underlying neural circuitries, including dopamine (DA) systems regulated by DA transporters (DATs) and vesicular monoamine transporters (VMAT2s). The current study evaluated striatal DAT function (uptake and methamphetamine-induced reverse transport), striatal DA D2 receptor density and food-motivated behavior in an animal model of diet-induced obesity (DIO). DIO was established by feeding rats a HF diet for 8 wks followed by segregation based on body weight into obesity prone (OP) and obesity resistant (OR) groups and compared to rats fed a low fat (LF) diet. Pre-existing differences in impulsivity and food-motivated behavior were evaluated also as predictors of the development of DIO. Results showed that Vmax for DAT in OP and LF groups was 42% and 35% lower, respectively, than for the OR group. Methamphetamine-evoked [^{3}H]DA overflow from OP striatum was 2-fold greater than in OR. DA D2 receptor density was 36% lower in OP compared to OR rats. OP exhibited a higher progressive ratio (PR) breakpoint for both HF and LF food reinforcement and greater resistance to extinction compared to OR, indicating increased motivation for food reward. A positive correlation was observed between PR breakpoint and subsequent body weight gain, suggesting that incentive motivation for HF food reward predicts the development of DIO. Taken together, the results suggest that a pre-existing elevation in motivation to obtain HF food predicts the development of DIO, which is subsequently associated with down-regulation of D2 receptors, reduced DA uptake by DAT, and enhanced DAT reverse transport, all of which would increase extracellular DA levels, further elevating the pre-existing augmented incentive motivation for food reinforcement and exacerbating the cycle of DIO.

Supported by: NIH P50 DA05312 (Linda P. Dwoskin), NIH HL73085 (Lisa A. Cassis) and a Predoctoral Fellowship from American Heart Association, AHA 715489B (Vidya Narayanaswami).
Primary Presenter / e-mail: Narayanaswami, V. / vnara2@email.uky.edu
Mentor or Senior Author / e-mail: Dwoskin, L. P. / ldwoskin@email.uky.edu

62 **Abstract Title: Developing a Weight Loss Intervention for Appalachian Adults: A Preliminary Survey**

Author(s): K.H. Webber, Department of Nutrition and Food Science, U of Kentucky
L. Quintiliani, Boston Medical Center

Abstract:
Introduction: The purpose of this research was to gather information for the design of a weight loss intervention for adults in Appalachian Kentucky. Methods: A random digit dialed phone survey was conducted with 404 adults in Appalachian Kentucky. Results: Most survey respondents were female (71%) and overweight or obese (69%) with an average age of 47.2 (11.8) years. Nearly half (48%) reported a diagnosis of a chronic health condition. The most common barriers to weight loss were current eating habits, time, and current physical condition. The most common motivators were health, appearance, and feeling better. Most respondents (68%) indicated interest in losing weight, with 40% preferring a face-to-face program. Females were more likely to have an accurate weight perception and a greater interest in weight loss than males. Conclusion: There is a need as well as a desire for weight loss programs among adults in Appalachian Kentucky, especially among females. Programs targeting males should focus on raising awareness of the problem before beginning.

Supported by: Univeristy of Kentucky Health Education throught Extension Leadership Grant
Primary Presenter / e-mail: Webber, K. H. / kelly.webber@uky.edu
Mentor or Senior Author / e-mail: Webber, K. H. / kelly.webber@uky.edu

63 **Abstract Title: HgA1c in Relationship to Patient Knowledge of Diabetic Complications: A Pilot Study**

Author(s): K.L. Bowling, Department of Family and Community Medicine - U of Kentucky -Hazard
J.E. Kingery, Department of Family and Community Medicine - U of Kentucky - Hazard
T.L. Knox, Department of Family and Community Medicine - U of Kentucky - Hazard

Abstract:
Background: The prevalence of diabetes (excluding gestational diabetes) in Kentucky has increased from 6.5% in 2000 to 9.9% in 2007. In 2007, 12% of Perry County adults reported diabetes compared to 7% of adults nationally. As a result of this increase in prevalence, many diabetic patients may be unaware of the complications linked to diabetes, which can include retinopathy, neuropathy, cardiovascular disease, and skin ulcers. Hypothesis: Knowledge of diabetic complications could result in lower HgA1C levels Methods: 30 participants (18 males, 12 females) with diabetes were asked to complete a survey regarding their awareness of diabetic complications. Results: A P value of 0.68 did not reveal significant differences between the two groups, but a smaller difference in the expected direction suggests a larger sample size may increase the power of the study. Conclusion: If diabetic patients were provided education on the increased severity of complications associated with poorly controlled diabetes, they may work harder to accomplish tighter glucose control. Increasing awareness of the complications of diabetes and the consequences of poorly controlled diabetes could have a substantial impact on patients' HgA1c levels. A larger sample size may help to definitely link HgA1c levels and awareness of diabetic complications in a rural, Appalachian population.

Primary Presenter / e-mail: Bowling, K. L. / klbo222@email.uky.edu
Mentor or Senior Author / e-mail: Kingery, J. E. / jeking0@email.uky.edu

64	**Abstract Title:**	**Policy Analysis: Is There a Relationship Between Required Physical Education in Lower Grades and Adolescent Obesity Rates? A Kentucky Case Study**

Author(s): D. A. Gross, Center for Excellence in Rural Health-Hazard, U of Kentucky

Abstract:

Background: Childhood obesity has emerged as a national epidemic. Yet, as of 2006, KY and seven other states - AK, CO, FL, MI, OK, OR and SD - did not require that physical education be taught in elementary or middle schools. The author hypothesized that states requiring PE in grades K-8 had lower rates of adolescent obesity. Methods: Data sources included the Youth Risk Behavior Survey (2007) and the School Health Policies and Programs Study (2006). The author conducted an independent t-test to determine whether a significant adolescent obesity rate difference existed between states (n = 43) that require PE in lower grades and states (n = 8) that do not. The author used a regression analysis and bivariate correlations to analyze associations between states' adolescent obesity rates and students' nutrition and physical activity behaviors. Results: No statistical difference was found between the two groups of states' adolescent obesity rates (p = .80). Significant associations were found between adolescent obesity rates and three personal behaviors: 1) watching television for 3+ hours per day (correlation coefficient = .736; p < .001); 2) meeting recommended levels of physical activity (correlation coefficient = -.468; p = .002); and 3) attending a PE class one or more times per week (correlation coefficient = -.391; p = .018). Conclusions: These findings suggest adolescent obesity is multifactorial. High school students' prior participation in required PE is only one of many aspects to consider. Any meaningful effort to address adolescent obesity must be broad in scope.

Primary Presenter / e-mail: Gross, D. A. / dagros3@email.uky.edu
Mentor or Senior Author / e-mail: Ewalt, J. A. G. / joann.ewalt@eku.edu

65	**Abstract Title:**	**Acanthosis Nigricans As A Clinical Marker For Insulin Resistance In Obese Children**

Author(s): R. Aswani, Department of Pediatrics, Marshall University, Huntington, WV
A.Lochow, Department of Pediatrics, Marshall University, Huntington, WV
Y. Elitsur, Department of Pediatrics, Section of Gastroenterology, Marshall University, Huntington, WV

Abstract:

Obesity has been recognized as a major risk factor for various diseases including cardiovascular, endocrine, and skeletal diseases. Insulin resistant diabetes mellitus type -2 (IR-DM2) in obese children is a major risk factor for developing diabetes mellitus and cardiovascular complications. Increased skin pigmentation around the neck and /or at the armpits (Acanthosis Nigricans) is a common finding observed in obese children.Obese children who attended the gastroenterology and the outpatient general clinics were prospectively recruited to the study. Demographic data, BMI value, and fasting serum levels of glucose, insulin, lipid profile (Cholesterol, TG, HDL, LDL), and liver enzymes were obtained at first visit in all children. The presence or absence of AN was also recorded. Insulin resistant was calculated (HOMA equation) in each child and was compared to the AN rate. A total of 54 children participated. The mean age was 13.01 3.5 and the Male: Female ratio was 1.6:1.0. The mean BMI was 32.85 ± 5.54. The mean cholesterol level, TG, HDL, and LDL were 162 ± 32, 130 ± 77, 40 ± 9, and 96 ± 25, respectively. Acanthosis nigricans was documented in 33 (61%) children, and IR-DM2 was found in 28 (51.8%) children. Only few children had abnormal aminotransferases. AN detected IR-DM2 in obese children with a Sensitivity of 72.4%, Specificity 52%, PPV- 63.6%, NPV- 61.9%, and the accuracy rate was 63.6%. Significant correlation was found between BMI and IR-DM2 (r=0.482) Conclusions: Acanthosis Nigricans is an adequate clinical marker to detect IR in obese children. Acanthosis Nigricans and BMI are associated with the development of IR-DM2 in obese children

Primary Presenter / e-mail: Aswani, R. / aswani@marshall.edu
Mentor or Senior Author / e-mail: Elitsur, Y. / elitsur@marshall.edu

66 **Abstract Title: The Role of Gender in Physical Self-efficacy and Balance Among High School Basketball Players**

Author(s): C. Silkman, Department of Rehabilitation Sciences, U of Kentucky
J.M. McKeon ,Department of Rehabilitation Sciences, U of Kentucky

Abstract:
Context: Physical self-efficacy is the measure of an individual's perceived physical capabilities. To our knowledge, there is no data as to how physical self-efficacy relates to the performance of functional postural control. Objective: To examine sex differences in physical self-efficacy expectations and to determine the relationship between physical self-efficacy and a measure of postural control. Patients or Other Participants: Fifty-seven high school basketball players (30 males, age=15 ±1.4, height=178.9 ±9.9 cm, mass=75.6 ±14.6 kg; 27 females, age=15 ±1.2, height=168.1 ±7.0 cm, mass=63.8 ±9.3) participating in interscholastic basketball. Interventions: Each participant completed the Physical Self-Efficacy scale (PSE), a 22-item Likert scale questionnaire with higher scores indicating higher level of self-efficacy. Each participant then completed 3 20-second trials of the Balance Error Scoring System (BESS) single-limb stance for each limb. The number of errors incurred during each trial were tallied and totaled for the BESS score. Results: The following results are presented as a median[range]. Males had a significantly higher PSE score than females (males: 103[80 to 127]; females: 97[78 to 108]; p=0.01). No difference existed between the sexes for BESS scores, (males median score was 15.5[0 to 52], females was 11[0 to 40], p=0.20). A weak, nonsignificant relationship (r=-0.17, p=0.21) between BESS error scores and PSE scores existed. Conclusions: The results of this study indicate that physical self-efficacy expectations as measured by the PSE do not relate to postural control as measured by the BESS. The postural control system may be too complex to predict through physical self-efficacy expectations alone.

Supported by: Pilot Funding from UK Center for Clinical and Translational Sciences
Primary Presenter / e-mail: Silkman, C. / carrie.silkman@uky.edu
Mentor or Senior Author / e-mail: McKeon, J. / jmedi2@email.uky.edu

67 **Abstract Title: Lessons Learned from Obesity Interventions in Appalachian and Rural Communities**

Author(s): M. J. Ickes, Department of Kinesiology and Health Promotion, U of Kentucky

Abstract:
One of the overarching goals of Healthy People 2020 is to achieve health equity, eliminate disparities, and improve the health of all groups. Unfortunately, within the Appalachian region of the U.S., eighty-one percent of the counties have been noted to incur higher rates of obesity compared to the national average. There are a variety of reasons for the disparity of obesogenic risk in Appalachian and rural communities. In addition to genetic factors, lack of nutritional knowledge among caregivers, limited access to health professionals, fewer opportunities for physical education in schools and physical activity in the community, and perceived lack of support play a major role in the development of obesity in this population. Considering these associated barriers, the Institute of Medicine has expressed an urgent need to initiate obesity interventions among diverse groups, which include Appalachian and rural communities. Therefore, the purpose of this presentation is to review existing obesity prevention and treatment interventions targeting Appalachian and rural communities that were published between 1986 and 2011. An abundance of interventions related to obesity prevention exist, but fewer exclusively target Appalachian and rural communities. A total of six interventions specifically targeting Appalachian communities and 18 targeting rural areas have been summarized; including behavioral, social, and environmental approaches with youth and adults. Recommendations are presented to enhance obesity interventions among potentially underserved populations, and further necessitate the need to target these at-risk groups.

Primary Presenter / e-mail: Ickes, M. J. / melinda.ickes@uky.edu
Mentor or Senior Author / e-mail: Ickes, M. J. / melinda.ickes@uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

68	**Abstract Title:**	**Association of serum Adiponectin and Post menopausal Hypertension in obese and lean women**

Author(s):

S. Faiz MD, Department of Internal Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington ,WV
Y. Gebregiorgis MD, Department of Internal Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington ,WV
R. Stanek, Department of Internal Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington ,WV
N. Santanam PhD, MPH, Department of Internal Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington ,WV
T. Gress MD, MPH, Department of Internal Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington ,WV
A.Yaqub FACP, FACE, Department of Internal Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington ,WV

Abstract:

Background: Low circulating levels of Adiponectin have been associated with metabolic syndrome, diabetes, and cardiovascular disease. Incidence of hypertension in women increases following menopause. Relationship between serum Adiponectin and post-menopausal hypertension has not been fully explored. Hypothesis: We intended to study the association between hypertension, menopausal status and serum Adiponectin. We hypothesized that, after adjustment of BMI, post-menopausal women with hypertension will have lower Adiponectin levels than their normotensive pre-menopausal and post-menopausal counterparts. Materials and Methods: We recruited 43 women in this cross sectional study conducted at Marshall University endocrinology clinic. Patients were stratified into 8 groups based on their menopausal status, BMI and presence of hypertension. Women with known diabetes, renal failure and cardiovascular disease were excluded. Serum total and high molecular weight (HMW) Adiponectin were measured by ELISA (ALPCO diagnostics, Salem, NH) and HMW-to-total Adiponectin ratio (HMWR) was calculated. Results: Serum Adiponectin was significantly lower in obese as compared to lean women (p-value was <0.02 for total Adiponectin, <0.0017 for HMW Adiponectin and <0.002 for HMWR).Women with higher Waist-to-hip ratio (WHR) had significant trend towards lower total and HMW adiponectin levels as compared to those with lower WHR(p 0.014 for total Adiponectin & 0.04 for HMW). There was no significant difference in total or HMW Adiponectin levels among various patient groups. The difference in HMWR among various groups could be explained by obesity, being lower in obese groups as compared to non-obese groups. Conclusion: We found that total, HMW Adiponectin and HMWR were significantly lower in obese women as compared to their non-obese counterparts. We also found that both total and HMW Adiponectin decreased with increasing WHR. We were unable to find any association between hypertension, menopausal status and serum Adiponectin.

Primary Presenter / e-mail: Santanam, N. / santanam@marshall.edu
Mentor or Senior Author / e-mail: Yaqub, A. / yaqub1@marshall.edu

69	**Abstract Title:**	**Does adding a summer booster to an after-school physical activity and nutrition education program decrease BMI accretion?**

Author(s):
SA Rose, College of Medicine, College of Public Health, University of Kentucky
LM Turner, College of Nursing, University of Kentucky
E Stines, College of Medicine, University of Maryland
MJ Lineberry, College of Public Health, University of Kentucky
S Chokshi, College of Medicine, University of Kentucky
J Conigliaro, School of Medicine, New York University
A Stromberg, Department of Biostatistics, University of Kentucky
J Perman, College of Medicine, University of Maryland

Abstract:

Research Objective School-based programs can decrease body mass index (BMI) accretion. However, studies suggest that non-school environments may contribute more to childhood overweight than school environments. Our objective was to assess mean BMI percentile change in children enrolled in a summer booster program added to their year-long after-school physical activity and nutrition education program, compared to children participating in the yearlong program alone versus control. We hypothesized that students in the summer program would have less BMI accretion than those in the after-school program alone or those in neither program. Study design Children enrolled in a year-long high intensity physical activity and nutrition education intervention were invited to participate in a five-week summer booster program during summer 2009 (SU09), consisting of three afternoons per week of physical activity and nutrition education. Our primary outcome was mean BMI percentile change, calculated as the difference in BMI percentile between Spring 2009 (SP09) and either Fall 2009 (FA09) or the completion of the SU09 program. Principal findings Of the 292 students enrolled at school during the 2008-2009 school year, 105 had a BMI > 85th percentile in SP09. 37 students enrolled in the HI program during the school year and 16 of these students enlisted in the SU09 program. The mean BMI percentile for students completing the SU09 program (n=12) was 94.8 in SP09 and 94.1 in FA09 (mean change= -0.63%, p=0.15). The mean BMI percentile for HI program students alone (n=19) was 88.0 in SP09 and 90.1 in FA09 (mean change= +2.2%, p=0.32). The difference between these two mean changes was not statistically significant (p=0.31). Of those with a BMI 85th percentile in no program (n=39), the mean BMI percentile was 93.7 in SP09 and 93.4 in FA09 (-0.38%, p=0.42). The difference between these no program and SU09 program students was not statistically significant (p=0.77). Conclusions SU09 program students achieved a larger mean BMI percentile decrease than HI program students alone or students with a BMI 85th percentile who were not enrolled in either program. Although not statistically significant, however, these findings are promising as there was a trend toward decreased accretion in SU09 students. Continued physical activity and nutrition education throughout the summer may maintain and improve gains made by such programs during the school year.

Supported by: Kentucky Diabetes Research Foundation

Primary Presenter / e-mail: Turner, L. / lmpede3@uky.edu
Mentor or Senior Author / e-mail: Perman, J. / jperman@umaryland.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

70	Abstract Title:	**Effect of an after-school physical activity and nutrition education intervention on elementary school attendance.**

Author(s):
S Rose, College of Medicine, College of Public Health, University of Kentucky
L Turner, College of Nursing, University of Kentucky
J Conigliaro, School of Medicine, New York University
M Lineberry, College of Public Health, University of Kentucky
E Stines, College of Medicine, University of Maryland
A Stromberg, Division of Biostatistics, University of Kentucky
J Perman, College of Medicine, University of Maryland

Abstract:

Background: We studied the effect of an after-school physical activity and nutrition education program on attendance in overweight children (Body Mass Index (BMI) > 85th percentile). Methods: Based on Fall 2008 BMI, students at three elementary schools (W, H, and A) participated in three intensity level interventions: 1) high (HI): twice weekly after-school program at W; 2) medium (MI): in-school physical activity, nutrition education, and non-food reward program at W and H; and 3) control: no intervention at A. Schools were socioeconomically similar with >80% of children qualifying for free or reduced lunch. Primary outcome was mean days absent. Results: 556 students (A=212, H=166, W=178) were included in the analysis. 46% at A, 48% at H, and 44% at W were overweight (p=0.78). 37 students at W enrolled in HI; 34 were overweight. Overall, students at A missed 9.0 days during the school year, compared to 7.7 at H, and 7.6 at W (p=0.08). Excluding students in HI, there was no significant difference in absences by BMI percentile at each school (overweight versus not: A=9.5 versus 8.5, p=0.31; H=7.3 versus 8.1, p=0.35; and W=7.3 versus 8.5, p=0.33). Among overweight students, those in HI missed significantly fewer days than students not in HI (HI=5.73, W=7.3, H=7.3, A=9.5, p=0.01). Conclusions: Overweight students in HI missed significantly fewer days than those not enrolled. Students receiving MI missed significantly fewer days than students not enrolled. This suggests that school-based programs promoting physical activity and nutrition contribute to higher attendance rates in elementary school students. Future goals include identification of reasons for this difference.

Supported by: R03 2008-2010 NIH Academic-Community Coalition for a School Based Prevention/Treatment Program

Primary Presenter / e-mail: Cheever, T. / tbchee0@uky.edu
Mentor or Senior Author / e-mail: Perman, J. / jperman@umaryland.edu

71	Abstract Title:	**Adipose tissue extracellular matrix and vascular abnormalities in obesity and insulin resistance**

Author(s):
M.L. Spencer, Department of Medicine, Division of Endocrinology, and the Barnstable Brown Diabetes and Obesity Center, U of Kentucky
R. Unal,Department of Medicine, Division of Endocrinology, and the Barnstable Brown Diabetes and Obesity Center, U of Kentucky
B. Zhu, Department of Medicine, Division of Endocrinology, and the Barnstable Brown Diabetes and Obesity Center, U of Kentucky
N. Rasouli, Division of Endocrinology, Metabolism and Diabetes, University of Colorado Denver School of Medicine
C. A. Peterson, College of Health Sciences, U of Kentucky
P. Kern,Department of Medicine, Division of Endocrinology, and the Barnstable Brown Diabetes and Obesity Center,U of Kentucky

Abstract:

We hypothesized that adipose tissue (AT) blood vessel density and extracellular matrix (ECM) changes play a role in insulin resistance; we examined angiogenesis and ECM deposition in subcutaneous AT of non-diabetic subjects. Candidate gene expression was examined in 60 subjects (BMI 19-41 kg/m2; SI 0.47-9.5 x10-4 min-1/¼U/ml) and immunohistochemistry (IHC) was performed in 8 lean insulin sensitive (L/IS, BMI<25, SI>2.65) and 8 obese-insulin resistant (O/IR, BMI>30, SI<2.65) subjects. CD31 (an endothelial marker) mRNA showed little correlation with BMI or SI. However, CD31 positive capillaries (by IHC) were decreased by 58% in O/IR compared to L/IS; in contrast, larger vessels, double stained for alpha smooth muscle actin (ASMA) and CD31, were increased by 70% in O/IR, accounting for the lack of change in CD31 expression with obesity [Figure 1]. IHC analysis of AT ECM components showed that both collagen (Col) V and VI were increased in O/IR AT but with different distributions. Col V was diffusely located in L/IS but mostly surrounded large ASMA-expressing blood vessels in O/IR. Elastin was reduced as a component of adipose ECM in O/IR (12% of area by IHC in L/IS, vs 5% O/IR, p<0.05). To examine adipocyte-macrophage interactions in vitro, adipocytes (from stem cells) were co-cultured with M1, M2a, and M2c macrophages. Col V and elastin were mostly expressed in adipocytes. In the presence of M2a and M2c alternatively activated macrophages, which account for 75% of macrophages in obese AT, adipocytes expressed 3-4x more Col V in vitro. These results suggest the ECM of O/IR subjects was more stiff and fibrotic, likely due to the increase in collagens and the decrease in elastin, with a decrease in capillaries and increase in larger blood vessels, which may promote hypoxia, infiltration of M2 macrophages, and further fibrosis.

Supported by: National Institutes of Health Grants DK-39176 and DK-80327 (P. A. Kern) and DK-71349 and AG-20941 (C. A. Peterson), General Clinical Research Center Grant M01 RR-14288 (N. Rasouli).

Primary Presenter / e-mail: Spencer, M. L. / mike.spencer@uky.edu
Mentor or Senior Author / e-mail: Kern, P. A. / philipkern@uky.edu

72 **Abstract Title: The Impact of Perceived Obesity Levels on Health Status in Women**

Author(s):
K.S. Lee, College of Public Health, U of Kentucky
J. Guo, College of Public Health, U of Kentucky
L. Crofford, Department of Internal Medicine, U of Kentucky
H.M. Bush. College of Public Health, U of Kentucky

Abstract:
Objective: The purpose of this study was to examine the association between health status, perceived weight, and body mass index (BMI). Methods: Women (n=8426) living in Kentuckywere included in this analysis. General health status was measured on a 5-point Likert scale and dichotomized. Perceived weight was measured using one item (How would you describe your current weight?) with responses based on a 4-point scale. Women were asked to provide height and weight, providing a BMI that was categorized into a four-level variable. Women were further classified according to the agreement of BMI and perceived weight (Group1: BMI=perceived weight; Group 2: BMI > perceived weight; and Group 3: BMI < perceived weight). Logistic regression was used to examine the relationship between general health status and these three groups after adjusting for covariates (age, marital status, race, education, job, depressive symptoms, current stress, chronic fatigue, and chronic pain). Results: Approximately half (53%) of the women fell into Group 1, 34% were in Group 2, and 13% were in Group 3. After adjusting for potential confounders, a significant association between perceived weight-to-BMI groups and general health status was observed. When compared to women in Group1, the estimated odds of poorer health was 30% higher (aOR=1.3, 95% CI [1.1-1.6]) for women in Group 2 and 60% higher (aOR=1.6, 95%CI [1.2-2.1]) for women in Group 3. Conclusion: Discrepancies between subjective and objective body weight are related to poorer general health status in women. Further studies will be needed to understand this observation and improve general health status in women.

Supported by: University of Kentucky
Primary Presenter / e-mail: Lee, K. S. / kyoung.lee@uky.edu
Mentor or Senior Author / e-mail: Crofford, L. J. and Bush, H. M. / heather.bush@uky.edu

73 **Abstract Title: Performance Characteristics of an Acute Bout of Fatiguing Exercise in Older Women**

Author(s):
B. Y. Hanaoka, Rheumatology, U of Kentucky
B. T. Symons, College of Health Sciences, U of Kentucky
D. Long, College of Health Sciences, U of Kentucky
C. Peterson, College of Health Sciences, U of Kentucky
L. Crofford, Rheumatology, U of Kentucky

Abstract:
Background: Fatigue is prevalent in the general population and is directly associated with functional dependence and activity limitations that impact quality of life. The purpose of this study was to induce skeletal muscle fatigue in healthy women using incremental isometric exercise in order to evaluate the relationships between subjective and objective measures of fatigue, pain and demographic data. Material and methods: 21 participants between 50 and 70 years of age were enrolled. Participants completed a demographic survey, the Multidimensional Assessment of Fatigue (MAF), Multidimensional Fatigue Inventory - Physical Fatigue Scale (MFI- PF), the Short Form 36 Physical Component (SF36-PC), the Short Form 36 Mental Component (SF36-MC), the VAS-Pain (VAS-P) and the acute bout of fatiguing exercise. Lean body mass was measured using total body Dual-energy X-ray Absorptiometry (DXA) scan, maximal voluntary isometric strength (MVIC) and VAS-P were measured immediately before and after the fatiguing exercise protocol, and during the recovery phase (12 minutes). Results: Participants' mean age was 56.7 years (SD=4.2) and lean body mass was 39074.6 grams. Baseline measures: mean pre-MVIC= 125.6 (SD=27.6), MAF= 11.1 (SD=9.3), MFI-PF=7.5 (SD=3.2), SF36-PC= 54.5 (SD=6.2), SF36-MC=53.4 (SD=5.7) and VAS-P= 8.5 (SD=14.1). The mean post-fatiguing protocol percent change MVIC (Post %MVIC) was -26.7% (11.8) and the recovery phase percent change MVIC was -17.7% (SD=9.8). The mean baseline VAS-P was 8.5 (SD=14.1), the post-fatiguing protocol VAS-P was 16.9 (SD=24) and the recovery VAS-P was 7.8 (SD=12.2). Pearson bivariate correlations indicated a strong correlation between pre-MVC and lean body mass (r=0.524, p=0.0148). No correlations were found between pre, post and recovery phase MVIC and the MAF, MFI-PF, SF36-PC, SF36-MC and the VAS-P. Conclusions: The performance characteristics of the acute bout of fatiguing exercise were as expected in healthy participants. This study demonstrates the acute bout of fatiguing exercise is effective in inducing fatigue in elder women, as measured by decreased MVIC. In this population MVIC measures did not correlate with instrumental measures of pain and fatigue. More studies are needed to assess predictors of fatigue in this population. The acute bout of fatiguing exercise may be a useful tool to objectively measure fatigue in patients with rheumatologic disorders, in whom fatigue is also prevalent and associated with functional dependence and activity limitations that impact quality of life.

Primary Presenter / e-mail: Hanaoka, B.Y. / byha222@uky.edu
Mentor or Senior Author / e-mail: Crofford, L. J. / ljcrof2@email.uky.edu

74	**Abstract Title:**	**Incidence and risk factors, and clinical saquelae associated with refeeding syndrome in medical and surgical intensive care unit patients**

Author(s):
K. M. Ruf, Department of Pharmacy Services, UK HealthCare
P. S. Winstead, Department of Pharmacy Services, UK HealthCare; Department of Pharmacy Practice and Science, U of Kentucky
D. A. Flomenhoft, Department of Internal Medicine and Pediatrics, U of Kentucky
B. L. Magnuson, Department of Pharmacy Services, UK HealthCare; Department of Pharmacy Practice and Science, U of Kentucky

Abstract:
Background: Refeeding syndrome describes metabolic changes that occur after a severely malnourished or critically ill patient begins to receive nutrition support. The syndrome manifests itself within days of refeeding as disturbances in phosphorus, potassium and magnesium. Complications of the syndrome can be serious and may include cardiac arrest, respiratory failure, and death. Therefore, refeeding syndrome may be a major determinant in inpatient outcomes including days of mechanical ventilation, length of intensive care unit (ICU) stay and disposition at ICU discharge. Refeeding syndrome has been well described in critically ill patients receiving parenteral nutrition. However, nutrition support in the ICU has fundamentally changed as it has undergone a pronounced shift from parenteral to enteral methods. Therefore, an accurate characterization of refeeding syndrome in an enterally fed ICU population must be established. Objectives: The current study aims to calculate the incidence of refeeding hypophosphatemia (RH) associated with enteral nutrition in a mixed medical and surgical ICU population. Factors associated with the development of RH will also be evaluated. Days of mechanical ventilation, ICU length of stay, and mortality at ICU discharge will be compared between those patients that do or do not develop RH. Methods: This retrospective review of medical and surgical ICU patients will include those patients on the nutrition support service census at UK HealthCare between August 2009-August 2010 who received enteral nutrition. A patient will be characterized as having RH if he or she develops a phosphorus <2mmol/L within 72 hours of receiving enteral nutrition. Patient characteristics including admitting diagnosis, BMI, prealbumin, enteral nutrition product, and significiant comorbities will be collected. Relevant outcomes including days of mechanical ventilation, ICU length of stay, and dispostition at ICU discharge will also be analyzed. Results and conclusion: Data collection and analysis is currently in progress.

Primary Presenter / e-mail: Ruf, K. M. / kmruf2@uky.edu
Mentor or Senior Author / e-mail: Magnuson, B. L. / blmagn0@uky.edu

75	**Abstract Title:**	**Understanding the Relationship between Incarceration and Obesity: Impacts on Community Health Resources**

Author(s):
M.L. Gates, Department of Family and Community Medicine, U of Kentucky
P. Jessa, College of Public Health, U of Kentucky

Abstract:
The highly controlled prison population is the only subpopulation in the U.S. federally mandated to have access to healthcare; yet, we know little about the health status of prisoners (offenders) and how their health impacts the general public. It is well documented that the majority of offenders return to their community, which in Kentucky is oftentimes a rural underserved area. It is believed that offenders have higher prevalence of diabetes and rates of obesity than the "free world", and the few studies conducted regarding correctional health have linked confinement and limited food choices to offenders returning to their communities more obese and with more severe diabetes. This study asked, do offenders increase excess body weight, adversely impacting their diabetes, while incarcerated, and do they exacerbate already overburdened community health resources? A population study conducted with the Kentucky Department of Corrections did not support the notion that incarceration impacts obesity and diabetes; however, findings suggested population differences (e.g., gender), despite similarities in healthcare. The obesity rate for women was 50% compared to 25.1% for men. There also were differences between African Americans and Caucasians women, whose obesity rates were 61.7% and 47.5% respectively. There were gender differences in chronic disease rates where 42.3% of obese men had at least one chronic disease compared to 66.5% of women. While prison may not adversely affect overall offender health, women faired far worse than men despite similar access to healthcare, raising questions about how they cope with incarceration and what they understand about health.

Supported by: Kentucky Corrections Health Services Network
Primary Presenter / e-mail: Gates, M. L. / mgates@email.uky.edu
Mentor or Senior Author / e-mail: Roeder, P. / roeder@email.uky.edu

76 **Abstract Title: Screening and Management of Obesity in Medicaid Recipients in Kentucky**

Author(s): S.A. Rose, College of Medicine and College of Public Health, University of Kentucky
Y. Gokun, College of Pharmacy, University of Kentucky
J. Talbert, College of Pharmacy, University of Kentucky
J. Conigliaro, School of Medicine, New York University

Abstract:
Background: Medicaid recipients have a higher prevalence of obesity and associated medical expenditures than non-Medicaid recipients. Kentucky has both a high prevalence of obesity and poverty. Physicians do not routinely perform guideline-concordant obesity care, including body mass index (BMI) documentation and weight loss counseling. We used Kentucky Medicaid Adult Patient survey data to assess physician screening for obesity, physician assistance with weight loss, and patient attempts to lose weight. We hypothesized that obesity screening and weight loss assistance are low overall, and that weight loss attempts are more likely in those assessed and counseled by physicians. Methods: We conducted a descriptive analysis using obesity-related questions from the 2009 and 2010 Annual Kentucky Medicaid Adult Patient Surveys. The surveys were randomly sent to 5,000 adult Medicaid patients. We excluded patients who were not receiving routine care and who were pregnant in the past year. Results: 907 (18%) patients in 2009 and 1,305 (26%) patients in 2010 returned surveys. Of these, 607 (67%) from 2009 and 868 (67%) from 2010 met criteria for analysis. Surveyed patients were 74% female, 90% white, 55% > 45 years of age, and 58% > a high school education. 47% were obese (BMI > 30), 27% were overweight (BMI 25 to <30), and 26% were normal weight (BMI 18 to <25). 91% of patients reported having their weight checked by their physician in the past six months. Only 47% of patients reported that their physician counseled about specific ways to lose weight. In both 2009 and 2010, this was higher among obese (57% and 72%), compared to overweight (34% and 40%) and normal weight (14% and 18%) patients ($p<0.01$ for both years). 54% of patients in 2009 (75% of obese, 48% of overweight, and 22% of normal weight) and 50% of patients in 2010 (72% of obese, 44% of overweight, and 19% of normal weight) stated they have attempted weight loss in the past six months ($p<0.01$ for both years). Patients who reported their doctors talked to them about ways to lose weight in the past six months were more likely to try to lose weight than those whose doctors had not talked to them about ways to lose weight (2009: 78% versus 40%, $p<0.01$; 2010: 76% versus 38%, $p<0.01$ Conclusions: Medicaid providers do not routinely counsel patients regarding ways to lose weight. Medicaid patients report more weight loss attempts if their physicians have talked to them about ways to lose weight. Medicaid providers may be missing opportunities to provide guideline-concordant obesity care to their patients. Future goals include analysis of the 2009 and 2010 Medicaid Provider Surveys to assess for correlations between physician and patient report of obesity care.

Primary Presenter / e-mail: Gokun, J. / ygo226@uky.edu
Mentor or Senior Author / e-mail: Conigliaro, J. / joseph.conigliaro@nyumc.org

77 **Abstract Title: D-Tagatose Reduces HbA1c in Type 2 Diabetes**

Author(s): K. Stutler, Department of Pharmaceutical Sciences, U of Kentucky
R. Lodder, Department of Pharmaceutical Sciences, U of Kentucky

Abstract:
A phase 3 study of D-tagatose as a monotherapy in Type 2 diabetes tested the hypothesis that a 15 g TID dose would reduce HbA1c. The trial was conducted at 34 sites in the U.S. and 23 sites in India. A total of 102 patients were enrolled at U.S. sites, and 254 patients were enrolled at India sites. The NEET (Naturlose(R) Efficacy Evaluation Trial) data show that D-tagatose was more effective in the U.S. population than in the Indian population, as the PP* patients in the U.S. who were treated with D-tagatose had a reduction in HbA1c of 0.4% at two months, 0.6% at six months and 1.1% at 10 months on therapy ($p<0.05$). The results showed a statistically significant ($p<0.05$) reduction in HbA1c levels of 0.4% at 10 months in relatively healthy people with diabetes (U.S. ITT LOCF, n=101 and Global PP, n=92)*. The reduction was even more pronounced among PP patients treated in the U.S., and the reduction in HbA1c generally increased over the 10 months patients were treated. Patients in the study had a low average randomization HbA1c of 7.5% globally. Decreases in HbA1c with drugs to treat Type 2 diabetes are dependent on the baseline HbA1c; the higher the baseline the greater the decrease (Bloomgarden et al, Diabetes Care, Volume 29 Number 9 September 2006). Generally, one would not expect large decreases in HbA1c if the mean HbA1c at randomization is 7.5%. Patients with HbA1c levels between 8.0% and 9.0% globally, which are at the high end of the inclusion criteria, showed 0.7% reduction on D-tagatose at 10 months of therapy (PP, not shown in table). This occurred in a subpopulation of patients using the drug per protocol, but was not with statistical significance ($p=0.09$) due to the small number of patients (n=30) with HbA1c values at those levels. Tolerability data are still being analyzed, but the number of patients with one or more treatment-emergent adverse events in the active group (163) was comparable to those reported in the placebo group (166). No serious adverse event was deemed to be treatment related. No episodes of hypoglycemia or pancreatitis were reported in NEET.

Supported by: Biospherics, Inc.
Primary Presenter / e-mail: Stutler, K. / kstuts25@yahoo.com
Mentor or Senior Author / e-mail: Lodder, R. A. / Lodder@uky.edu

78 **Abstract Title: Identification of a FBN1 Isoform Sufficiently Abundant to Modulate Marfan Syndrome**

Author(s): M. Burchett, U of Kentucky College of Medicine
I. Ling, Department of Physiology, U of Kentucky
S. Estus, Department of Physiology, U of Kentucky

Abstract:
BACKGROUND: Mutations in FBN1 cause Marfan syndrome, a heritable disorder of connective tissue. FBN1 encodes the extracellular matrix protein, fibrillin. Our objective was to elucidate the extent that variation in splicing contributes to FBN1 mRNA isoforms. METHODS: To identify splice variants of FBN1 mRNA, we scanned each of its 64 internal exons in a set of pooled human brain cDNA samples. We then quantified expression in multiple tissues, including adult human skeletal muscle and brain, as well as fetal human skeletal muscle, brain, liver, aorta, lung, skin, and heart by using real time PCR. RESULTS: We report that FBN1 splicing is generally efficient as we identified only two splice variants, which include (i) a novel isoform containing a 105 basepair insertion between exons 54-55 (54A-FBN1) and (ii) a previously identified isoform (57A-FBN1) which contains a cryptic exon between exons 57 and 58. Quantification revealed that 57A-FBN1 represents 8-44% of FBN1 mRNA and varies in a tissue- and development-specific fashion. In fetal tissue, the proportion of 57A-FBN1 was high in brain (27%) and low elsewhere, e.g., skin, aorta and lung. In adult tissue, 57A-FBN1 represented 39 ± 3 (%, mean ± SD) of FBN1 mRNA in brain, and 19 ± 2 (%, mean ± SD) in skeletal muscle. CONCLUSIONS: A significant proportion of FBN1 is expressed as the 57A-FBN1. Since the 57A insertion creates a premature stop codon that mimics Marfan-associated mutations, the protein encoded by 57A-FBN1 is likely to be non-functional. These results suggest that altered splicing may regulate FBN1 expression, modulate disease severity, and, potentially, represent a therapeutic target.

Supported by: UK Center for Clinical and Translational Science
Primary Presenter / e-mail: Burchett, M. / mary.burchett@uky.edu
Mentor or Senior Author / e-mail: Estus, S. / sestus2@email.uky.edu

79 **Abstract Title: The Genetic Core Facility at Marshall University**

Author(s): G. Boskovic, Dept. of Biochemistry and Molecular Biology, Joan C. Edwards School of Medicine, Marshall U.
J. Denvir, Dept. of Statistics, West Virginia University
J. Fan, Dept. of Biochemistry and Molecular Biology, Joan C. Edwards School of Medicine, Marshall U.
J. H. Kim, Dept. of Pharmacology, Physiology and Toxicology, Joan C. Edwards School of Medicine, Marshall U.
D. A. Primerano, Dept. of Biochemistry and Molecular Biology, Joan C. Edwards School of Medicine, Marshall U.

Abstract:
Next generation sequencing and microarray applications require sophisticated method, expensive instrumentation and reagents and intense data management and analysis. These tasks are most efficiently executed in a core facility setting with expertise in genomic methods biostatistic and bioinformatics The Genomics Core Facility provides the following services to researchers at Marshall, WVU, WV-INBRE partner institutions and other institutions: (1) Next Generation Sequencing applications including, whole genome sequencing (resequencing and de novo sequencing), RNA-Seq, Chip-Seq, small RNA-Seq, metagenomics, exom sequencing, and bi-sulfide sequencing; (2) microarray-based gene expression profiling and other microarray applications, including bioinformatic and biostatistical support for microarray analyses; (3) automated DNA sequencing and genotyping and access to sequence analysis software; and (4) access to real-time thermal cyclers for quantitative PCR and to Agilent 2100 Bioanalyzers for DNA/RNA quantitation and quality assessment.

Supported by: NIH award RR 016477
Primary Presenter / e-mail: Boskovic, G. / gboskovi@marshall.edu
Mentor or Senior Author / e-mail: Primerano, D. A. / primeran@marshall.edu

80 **Abstract Title: Mapping Your Community: A Public Health Vision for Healthy Living**

Author(s): K. N. Farley, MS, Kanawha-Charleston Health Department, Charleston, WV
N. Vermillion, Kanawha-Charleston Health Department, Charleston, WV
R. Gupta, Kanawha-Charleston Health Department, Charleston, WV

Abstract:

The Appalachian region includes parts of twelve states and all of West Virginia with about 42% of the population living in rural areas which have many environmental barriers to physical activity. The region contains a disproportionate number of retired, disabled, unemployed and poor people and have higher than national rates of obesity and chronic diseases. The Kanawha-Charleston Health Department began to identify physical activity opportunities in 2007 and the process included formulating a database of opportunities through online searches, yellow pages, tourism guides, environmental scans and citizen referrals. The data was utilized as part of the Keys 4 HealthyKids initiative which is a Robert Wood Johnson Foundation Healthy Kids Healthy Communities grantee to identify areas that have little or no physical activity opportunities and make citizens aware of the opportunities in the areas they live, learn and work. The identified sites where then geocoded to provide accurate coordinates for future use and mapped using a basic web-based map service. A hardcopy map was also designed to reach citizens without internet access. The process identified one-hundred and fifty opportunities and the map provided citizens an opportunity to explore their communities from street level to community, city and county level. The maps were analyzed and two communities within one city were compared and provided a very dramatic demonstration where one area had opportunities within a few blocks the other went for miles without any opportunities. The map analysis information will be utilized for community outreach, city planning, policy change and support of environmental improvements to ensure all citizens have an equal opportunity to be active.

Supported by: www.kchdwv.org www.keys4healthykids.org
Primary Presenter / e-mail: Farley, K. N. / Krista.N.Farley@wv.gov
Mentor or Senior Author / e-mail: Gupta, R. / Rahul.Gupta@wv.gov

81 **Abstract Title: Screening for Lung Disease in Primary Care Practices**

Author(s): D. Mannino, MD, College of Public Health, U of Kentucky
R. Copeland, College of Public Health, U of Kentucky
L. Rogers, College of Public Health, U of Kentucky
D. Valvi, MD, College of Public Health, U of Kentucky
S. Mittenzwei, College of Public Health, U of Kentucky

Abstract:

The objective of the research is to look at the relationship between the resources and information doctors at various clinics are given and the diagnosis and treatment patients receive. Our hypothesis is that, when more information is received, the diagnosis and treatment will be done more promptly. The poster will mostly focus on the study design, as well as recruitment and IRB issues, as the study is still in progress. The expected end date of the study is mid-May, with the analysis of data following through the summer and fall of 2011.

Supported by: Boehringer Ingelheim, Pharmaceuticals.
Primary Presenter / e-mail: Mannino, D. / dmannino@uky.edu
Mentor or Senior Author / e-mail: Mannino, D. / dmannino@uky.edu

82 **Abstract Title:** **Vitamin D: Evaluation of Current Practices in a University-Based Primary Care Clinic**

Author(s): C. McKee, College of Medicine, University of Kentucky
K. Bennett, Department of Family and Community Medicine, University of Kentucky
Margaret Love, Department of Family and Community Medicine, University of Kentucky

Abstract:
HYPOTHESIS: The objective of this study is to determine current practices of health care providers and patient experience regarding vitamin D discussion, testing, and recommendations in an academic primary care clinic. Low numbers of patients reporting vitamin D discussion were anticipated. PROCEDURES: The study has 2 components: (1) Secondary analysis of existing data from patients participating in a quality improvement survey and (2) a provider survey. Patients in the Family Medicine clinic's waiting room were invited to complete a pre- and post-visit waiting room survey. Providers in the same clinic will be invited to complete the anonymous survey on-line. Instruments used included: (1) Patient survey covering demographics, reason for visit, and interactions with providers concerning vitamin D and (2) Provider survey about their vitamin D practices. Main outcome measures included: (1) Frequency of positive vitamin D encounters, in which patients reported that vitamin D was discussed. (2) Provider practices concerning vitamin D; and relations between provider practices and characteristics. (3) Comparisons between patient-reported experience and provider-reported practices. PARTICIPANTS: (1) 136 adult patients and parents. (2) All physicians and nurse practitioners in the clinic will be invited to complete the provider survey. ANTICIPATED RESULTS: Low numbers of visits with vitamin D discussion were reported by patients. Similar results are expected from the provider survey. CONCLUSION: Low frequency of positive vitamin D encounters indicates the need for interventions to improve provider and patient education about vitamin D.

Supported by: Department of Family and Community Medicine, University of Kentucky University of Kentucky College of Medicine
Primary Presenter / e-mail: McKee, C. / candace.mckee23@uky.edu
Mentor or Senior Author / e-mail: Bennett, K. / keisa.bennett@uky.edu

83 **Abstract Title:** **Social Support as a Moderator of Perceived Relationship Power and Mental Health Symptoms in a Sample of Incarcerated, Substance Using Women with a History of Intimate Partner Violence**

Author(s): A. M. Minieri, College of Social Work, U of Kentucky
M. Staton-Tindall, College of Social Work, U of Kentucky
C. Leukefeld, Department of Behavioral Science, U of Kentucky

Abstract:
Research has shown social support is a protective factor for women who have experienced intimate partner violence (IPV), decreasing the effect of the victimization on subsequent mental health symptoms (e.g. Coker et al., 2002; Mitchell et al., 2006). Relationship power has also been shown to influence this association (Filson et al., 2010). Less is known, however, about how social support and perceived relationship power are associated with mental health among victims of IPV. Therefore, the purpose of this study was to examine whether social support moderates the relationship between perceived relationship power and mental health symptoms among 304 incarcerated women with a history of substance abuse and IPV. It was hypothesized that perceived relationship power and mental health symptoms would be significantly associated among IPV victims who reported low social support but not high social support. Most participants identified as Caucasian, completed high school, and their median age was 35. Exploratory analyses indicated that among women who reported low social support, perceived relationship power significantly predicted mental health symptoms, $F(1, 137) = 5.028$, $p = .027$, with perceived relationship power having a statistically significant regression weight, $t(137) = -.625$, $p = .027$, supporting this hypothesis. However, perceived relationship power did not predict mental health symptoms among women who reported high social support, $F(1, 148) = 3.380$, $p = .068$. This finding suggests high social support may be protective against the negative effects of perceived relationship power on mental health symptoms and should be considered in treatment planning for these women.

Supported by: The National Institute of Drug Abuse (NIDA) Criminal Justice Drug Abuse Treatment Studies (CJ-DATS) cooperative agreement
Primary Presenter / e-mail: Minieri, A. M. / alexandra.minieri@uky.edu
Mentor or Senior Author / e-mail: Staton-Tindall, M. / mstindall@uky.edu

84 **Abstract Title:** **Retaining Future Physicians in the Commonwealth: Current Residents' Intent to Practice in Kentucky**

Author(s):
G. S. Munday, U of Kentucky College of Medicince
A. Morgenstein, U of Kentucky College of Medicince
Emery A. Wilson, MD, Interim Dean, Office of Medical Education, U of Kentucky College of Medicince
Carol Elam, PhD, Office of Medical Education, U of Kentucky College of Medicince
Elmer Whitler, MA, MPA, Office of Health Research and Development, U of Kentucky College of Medicince

Abstract:
Objectives: 1) estimate the percentage of University of Kentucky College of Medicine (UKCOM) resident physicians that plan on practicing in Kentucky after training; 2) understand impact of selected influences on the decision of practice location; and 3) identify social and demographic indicators of residents who plan to practice in Kentucky. Methods: A 12 item online questionnaire was used to collect information on a voluntary basis from the current 545 UKCOM resident physicians during a two-month period. The questionnaire collected information on post graduate year, social and demographic characteristics, medical specialty, practice type and location, and factors that influenced the anticipated practice location. Chi-square and Kendall's tau-b were used to test categorical and ordinal variable relationships respectively. Results: Approximately half of the residents surveyed are undecided about whether they want to practice in Kentucky upon completion of their training. Social and demographic characteristics that had a significant correlation ($p<0.05$) with planning to practice within the Commonwealth were: female gender; being in a primary care specialty; having previous educational training in Kentucky; residents with more levels of education completed in Kentucky were more likely to want to stay to practice; and wanting to practice in a rural classified community. Factors that had a significant correlation ($p<0.05$) with the decision of practice location were commitment to serve Kentuckians and state income taxes. The correlation of the medical liability environment approached significance ($p=0.118$). Conclusion: The Commonwealth has a large need for physicians and uses a large amount of resources educating its residents each year. These findings suggest social and demographic characteristics that could be used in the selection of resident physicians that would be more likely to practice in Kentucky after training. Retaining more physicians for Kentucky must be a collaborative effort from the Commonwealth's residency programs, hospitals, and healthcare policy makers.

Supported by: Emery Wilson Enrichment Grant
Primary Presenter / e-mail: Munday, G. S. / swope.munday@uky.edu
Mentor or Senior Author / e-mail: Wilson, E. / ewilson@uky.edu

85 **Abstract Title:** **Impact of Autoimmune Disease on Health Status and Health Care Utilization: Cross-Sectional Data from the Kentucky Women's Health Registry**

Author(s):
P. S. Poynter, medical student, U of Kentucky
L. Crofford, Department of Internal Medicine
H. Bush, College of Public Health, U of Kentucky
K. S. Lee, nursing student

Abstract:
Background: A number of studies have looked at subgroups of autoimmune diseases and remarked about mood disorders and health-related quality of life. We compare the autoimmune population as a whole to healthy controls as well as women with other chronic diseases in an attempt to see if the presence of a systemic autoimmune disease is an independent indicator of poor health-related quality of life outcomes. Methods: This study includes cross-sectional data from the IRB approved Kentucky Women's Health Registry during the years 2006-2008. Healthy controls did not identify having the autoimmune diseases selected nor did they indicate having asthma or hypertension. A total of 10,684 women were included in the overall study with 794 of those having one or more systemic autoimmune diseases. Results: Odds ratios were adjusted for age, education, race, employment, smoking status, marital status, insurance, Appalachian residence, social support, depression, anxiety, sedentary life style, BMI, and total medical comorbidities. The adjusted odds ratio for having poor perceived health was 4.492 (95% CI 3.431-5.881) in the autoimmune population with healthy controls as the reference value. Both asthma and hypertension cohorts had an adjusted odds ratio of 1.7 for poor perceived health and confidence intervals did not overlap with the autoimmune cohort. Chronic fatigue and pain adjusted odds ratios were also significantly higher among the autoimmune cohort than the other cohorts. Conclusions: Women with autoimmune diseases tend to fare more poorly on a variety of health-related quality of life measures, specifically poor perceived health status, chronic fatigue, and chronic pain.

Supported by: PSMRF
Primary Presenter / e-mail: Poynter, P. S. / pspoyn2@uky.edu
Mentor or Senior Author / e-mail: Crofford, L. J. / ljcrof2@email.uky.edu

86 **Abstract Title: Quantitative Analysis Assessing Health Risks of Emergency Department Shift Workers**

Author(s): S. Desai, Department of Emergency Medicine, University of Kentucky
M. Hicks, Medical Student
E. Dearing, Medical Student

Abstract:

Purpose: With the growing interest in the effect that shift-work has on the body, the purpose of the study was to quantitatively measure blood pressure to address the impact that disturbances in the circadian rhythm have on the cardiovascular system and, thus, overall health. Design: This study is a prospective research project. Setting: The study took place in a teaching, urban, level I trauma center, which saw an average of about 60,000 total patients (adult and pediatric) this past year. The nursing staff that participated in the study staffs all pods of the emergency department. Participants/Subjects: Participants were selected on a voluntary basis. All registered nurses or nurse technicians employed in the university emergency department were eligible for participation. The subjects were adults with 36 females and 8 males. The subjects were able to volunteer during their shift, which was either day (7a-7p) or night (7p-7a). The night nursing staff had an average age of 28.66 as compared to the day nursing staff average age of 34.34. Data was gathered for eight total days, which allowed most of the subjects to be tested during multiple shifts. Of note, the day and night nursing staff always work their respective shifts. Methods: Participants from each of the five pods randomly volunteered at the beginning of each working shift, with the minimum number of subjects per shift equal to five (one for each pod). On the first day of gathering data for a particular subject, they were asked to fill out a consent and a survey with basic demographic information as well as pertinent cardiovascular past medical and social histories (e.g. hypertension, diabetes, hypercholesterolemia, smoking and alcohol intake) and various stress-related questions (e.g. any regular exercise or stress-relieving activities). Each participant's blood pressure with pulse was then measured at the beginning, middle, and end of shift using a mobile machine on the same arm, if possible. The mobile machine that was used for a certain participant was the same machine used for the remainder of the measurements for that particular shift and participant. If a participant was working on a subsequent data-gathering shift, they were enrolled again for that shift on a voluntary basis. Results/Outcomes: A two-tailed, two-sampled, unequal variance T- test was used to compare night shift and day shift results. Systolic, Diastolic and Heart Rate values were compared across all subjects. Comparisons were made based on the beginning, middle, and end of shifts. Assuming a significant p Value of .05, none of the variance between day and night shifts proved to be statistically significant. Implications: From the study, it was concluded that shift-work has no statistically significant effect on blood pressure for nursing staff that do not rotate their shifts (i.e. night nurses always working night shift). Future studies need to be completed to compare the nursing staff to emergency department staff that does rotate shifts (e.g. residents).

Supported by: PSMRF funding
Primary Presenter / e-mail: Hicks, M. D. / hicks.matthew@uky.edu
Mentor or Senior Author / e-mail: Desai, S. / sameerdesai00@gmail.com

87 **Abstract Title: Local Health Departments Quality Improvement Efforts in Preparing for Voluntary Accreditation**

Author(s): J.L. Wehle, Health Services Management, U of Kentucky

Abstract:

Objectives: To determine why some local health departments (LHD) have Quality Improvement (QI) programs in place while other do not. To determine the QI framework LHD choose to implement. Methods: Analyze the responses of LHD to the QI module questions asked in the 2008 NACCHO Profile Survey questionnaire. The core survey instrument was sent out the 2,794 local, tribal and state health departments and of those the QI module was administered to 545 health departments. Analysis: Descriptive statistics and bivariate analysis were completed on the sample of 448 LHD respondents of the QI module. Results: There is a positive association between the jurisdiction size and undertaking QI efforts. The analysis showed a trend towards association for LHDs with QI efforts in the last two years seeking accreditation eventually. No significant association ($p > 0.5$) was determined for LHDs with QI efforts in the last two years seeking accreditation within two years. Analysis of whether LHDs within a geographic area implement similar QI framework showed there was a lack of QI framework implementation within the southeastern region. Conclusion: Additional empirical research is needed for PHAB accreditation standards, quality improvement utilization, and accountability and performance management. Tools and programs are needed to aid small LHDs (<50,000) in their efforts to implement appropriate QI framework. The voluntary accreditation would promote a systematic implementation of QI and PM into the LHD structure.

Supported by: U of Kentucky College of Public Health
Primary Presenter / e-mail: Wehle, J. L. / jessica.w@uky.edu
Mentor or Senior Author / e-mail: Costich, J. F. / jfcost0@uky.edu

88 **Abstract Title:** **Impact of an Emergency Medicine Clinical Pharmacist on Phenytoin Dosing in a University Teaching Hospital**

Author(s): A. L. Rogalski, Department of Pharmacy Services, UK HealthCare
S. N. Baker, Department of Pharmacy Services, UK HealthCare
M. M. Hall, Department of Emergency Medicine, UK HealthCare
J. E. Martin, Department of Emergency Medicine, UK HealthCare
A. M. Cook, Departments of Pharmacy Services, UK HealthCare, and Pharmacy Practice and Science, U. of Kentucky
G. A. Davis, Departments of Pharmacy Services, UK HealthCare, and Pharmacy Practice and Science, U. of Kentucky
K. A. Weant, Department of Pharmacy Services, UK HealthCare

Abstract:
Phenytoin is a commonly used antiepileptic in the emergency department for new onset epilepsy, status epilepticus, and the prevention of post-traumatic epilepsy. HYPOTHESIS: Phenytoin loading doses more often achieve concentrations within the therapeutic range when a clinical pharmacist is present and involved in their emergency department (ED) care than during the hours not covered by a dedicated clinical specialist. METHODS: Retrospective analysis of patient charts is underway. Adult patients were selected who presented to the ED and received IV phenytoin or fosphenytoin between April 2006 and April 2010. Patients receiving IV loading doses were evaluated for achievement of post loading concentrations within the therapeutic window. Albumin adjusted phenytoin concentrations within the range of 10-20 mcg/mL were considered therapeutic. Compliance with loading doses in the range of 15-20 mg/kg, frequency of appropriate post-load concentration orders, optimal re-dosing if concentrations are subtherapeutic, and optimal maintenance dosing will be assessed secondarily. Analysis will be performed based on the presence of an Emergency Medicine specialist or resident who is present from 1 PM to 11 PM, seven days per week. Doses administered during these times will be compared to those during the absence of a pharmacist. RESULTS: Current analysis of data indicates that when a pharmacist is present in the ED, therapeutic concentrations of phenytoin are achieved in 81 of 109 patients using an average loading dose of 17.2 mg/kg, with an additional 11.1% achieving concentrations between 20-25 mcg/mL. CONCLUSIONS: Preliminary analysis is limited, though chart review is anticipated to be complete at the time of presentation. The available data suggest that patients receiving phenytoin loading doses when a pharmacist is present are highly likely to achieve therapeutic concentrations.

Supported by: UK College of Pharmacy
Primary Presenter / e-mail: Rogalski, A. L. / alro225@uky.edu
Mentor or Senior Author / e-mail: Weant, K. A. / kawean2@uky.edu

89 **Abstract Title:** **Project GO! Web Based Learning for Improved Childhood Health Behaviors: A Catholic Elementary School Pilot**

Author(s): R. L. Hoisington, UK REACH Liaison, Madisonville, KY
K. H. Webber, Department of Nutrition and Food Science, U of Kentucky
S. G. Bosaw, Department of Juvenile Justice, Madisonville, KY

Abstract:
This project is a work in progress collaboration between the University of Kentucky and the interested community within the UK Research and Engagement for Advancing Community Health (REACH) Madisonville region. The community realizes the tremendous need to instill lifelong healthy lifestyle habits into their youth population. Currently, Union County Kentucky is grossly above the national average in adult obesity, lack of physical activity, adult diabetes, cardiovascular deaths, cancer deaths, and total mortality. This study wishes to pilot a novel web based health and nutrition teaching platform named Project GO! in the St. Ann Catholic School 2nd - 5th grade population consisting of 115 students. The web program will provide these students with 15 hours of educational content broken down into five modules: fast food, healthy drink choices, screen time, physical fitness, and fruits/vegetables. Primary Objective: Does administering Project GO! to 2nd - 5th graders at St Ann Catholic School meaningfully improve health behaviors related to the five program modules vs. a similar student population at a control Catholic School? Secondary Objective: To determine the overall perception and acceptance of the program by students, teachers, parents, and school administration. Methods: Fall 2011 throw motivational kick off party at both study and control schools. November 2011 deliver informational packets to caregivers about Project GO! and offer ability to use Project GO! at home plus track their child's progress through e-mails. Jan 1st 2012 start Project GO! with baseline health assessments on both school groups. Run three modules in spring 2012 and two modules in fall 2012 with student surveys following module completion. Reassess baseline health assessments at both schools Jan 2013 then wrap up with data analysis and student, teacher, caregiver focus groups.

Supported by:
Primary Presenter / e-mail: Hoisington, R. L. / rhoising@trover.org
Mentor or Senior Author / e-mail: Webber, K. H. / khwebb2@email.uky.edu

90 **Abstract Title: Quality of Depression Care in Kentucky**

Author(s): S. R. Botts, Institute of Pharmaceutical Outcomes and Policy, Department of Pharmacy Practice & Science, U of Kentucky
G. Liu, Institute of Pharmaceutical Outcomes and Policy, Department of Pharmacy Practice & Science, U of Kentucky
J. C. Conigliaro, NYU-HHC Clinical and Translational Science Institute, Division of General Internal Medicine, New York University
J. Talbert, Institute of Pharmaceutical Outcomes and Policy, Department of Pharmacy Practice & Science, U of Kentucky

Abstract:
Purpose: To determine the extent of guideline-concordant depression care and identify variables associated with receipt of quality care. Methods: Retrospective evaluation using a large administrative claims database. Subjects include Kentucky Medicaid enrollees with a new episode of depression and 12 months of continuous eligibility during the time period of January 2000 - December 2007. Guideline concordant care was defined as 1) receipt of an antidepressant within the first 84 days and a medication possession ratio 80% during first 6 months or, 2) receipt of psychotherapy within 30 days of the index episode and at least 2 treatments within 84 days. Explanatory variables included; subject demographics, care setting and location, comorbidity, rural and Appalachian residence. Results: Of the 31,624 depression episodes evaluated, 46% of subjects reside in rural Appalachian counties. Thirty percent of subjects received an antidepressant while 4.2% had adequate supply of medication during the first 6 months. Thirteen percent of subjects received adequate psychotherapy. Follow-up visits increased the odds of receiving adequate antidepressant treatment (OR 1.87, 95% CI 1.62-2.14), as did comorbid diabetes (OR 1.18, 95% CI 1.01-1.38) and white race (OR 1.84 95%CI 1.4-2.4). Male gender (OR 0.8 95% CI 0.7-0.91), age 19-24years (OR 0.51, 95% CI 0.42-0.64), and prior depressives episodes (OR 0.33, 95% CI 0.27-0.42) decreased the odds of receiving antidepressant therapy. Treatment at a CMHC increased the odds of receiving psychotherapy (OR 1.2, 95% CI 1.02-1.19). Appalachian residents were less likely to receive psychotherapy (OR 0.84 95% CI 0.74-0.96). Conclusion: Less than one of five Medicaid enrollees received adequate treatment for depression. Appalachian residents and those receiving care at CMHC's were more likely to receive psychotherapy. Consistent with other literature, comorbid diabetes, white race, and follow-up care increased adequate antidepressant treatment.

Supported by: UK Center for Clinical and Translational Science Pilot Award
Primary Presenter / e-mail: Botts, S. / sbott2@email.uky.edu
Mentor or Senior Author / e-mail: Talbert, J. / jtalb1@email.uky.edu

91 **Abstract Title: Emergency Pharmacist Impact on HealthCare Associated Pneumonia Empiric Therapy**

Author(s): S.R. DeFrates, Department of Pharmacy Services, U of Kentucky
S.M. Baker, Department of Pharmacy Services, U of Kentucky
K.W. Weant, Department of Pharmacy Services, U of Kentucky

Abstract:
Background: Emergency Medicine physicians must frequently make the distinction between community acquired (CAP) and health care associated pneumonias (HCAP) in order to provide appropriate empiric antimicrobial therapy. Emergency medicine pharmacists (EPh) have the knowledge necessary to evaluate patients for risk factors associated with HCAP and the skills needed to initiate appropriate antimicrobial therapy at optimal doses. By having EPh involved directly in the care of these patients, we anticipate an improvement in appropriateness and timeliness of therapy. Objectives: The primary objective of this study is to evaluate the impact of the EPh on the identification of patient risk factors for HCAP by evaluating the appropriateness of empiric antibiotic therapy. Secondary objectives are to determine if the EPh affects empiric dosing of antibiotics, time to administration of antibiotics and if appropriate antibiotic therapy affects intensive care unit length of stay (LOS) and hospital LOS. Methods: This will be a retrospective chart review of patients who presented to the Emergency Department (ED) between September 1, 2008 to June 30, 2010. Two study groups will be assessed, the control group will be those HCAP patients who presented to the ED outside of the EPh hours (23:00-13:00), and the study group will consist of those patients who presented during the EPh shift (13:00-23:00). Assessment of appropriateness of therapy will be determined by the ATS/IDSA guidelines, the University of Kentucky antibiogram, and a panel of infectious disease experts. Results: Study in progress Conclusion: Study in progress

Supported by:
Primary Presenter / e-mail: DeFrates, S. R. / sean.defrates@uky.edu
Mentor or Senior Author / e-mail: Baker, S. M. / stephnbaker@uky.edu

92 **Abstract Title:** **Susceptibility of Escherichia coli to Ampicillin-Sulbactam in Community-Acquired Intra-Abdominal Infections and Outcomes Associated with Its Use**

Author(s): J. G. Bekker, Department of Pharmacy Services, U of Kentucky
C. A. Martin, Department of Pharmacy Services, U of Kentucky
S. N. Baker, Department of Pharmacy Services, U of Kentucky
P. A. Kearney, Department of Surgery, U of Kentucky
K. E. Record, Department of Pharmacy Services, U of Kentucky

Abstract:
Background: Complicated intra-abdominal infections are primarily managed through surgical intervention and adjunctive antibiotic therapy. Guidelines published in 2003 by the Infectious Diseases Society of America (IDSA) and Surgical Infection Society (SIS) recommended using ampicillin-sulbactam for complicated community-acquired infections of mild-to-moderate severity, with the caveat that local Escherichia coli (E. coli) susceptibility profiles should be examined prior to antibiotic selection. However, the 2010 IDSA/SIS guidelines recommend against its use due to widespread E. coli resistance. Objectives: The primary objective was to identify the resistance of E. coli to ampicillin-sulbactam in this patient population and how it compares to the data referenced in the guidelines and overall hospital antibiograms. The secondary objective was to determine whether laboratory resistance to ampicillin-sulbactam reflects clinical efficacy in vivo. Methods: Patients were identified for inclusion using ICD-9 diagnosis codes in the University HealthSystem Consortium (UHC) Clinical Data Base and screened for final inclusion via retrospective chart review. Adult patients admitted to our institution from January 2007 to December 2009 were included if they were admitted from the community, had a complicated intra-abdominal infection requiring surgical intervention, had been in the hospital <48 hours at infection onset, had cultures obtained during surgery positive for E. coli, and received at least one dose of an antibiotic. The ampicillin-sulbactam susceptibility of E. coli isolated in the study population was compared to that reported in the institution's antibiogram. Outcomes were evaluated for patients who received ampicillin-sulbactam after surgery and whose cultures were positive for resistant E. coli versus susceptible E. coli. Results/Conclusions: In the 2007-2009 antibiograms, 52% of 5586 E. coli isolates were susceptible to ampicillin-sulbactam. Approximately 39 patients must be identified for the study population to detect a 25% difference between groups with a power of 90%. Data analysis and conclusions are in progress.

Primary Presenter / e-mail: Bekker, J. G. / jenny.bekker@uky.edu
Mentor or Senior Author / e-mail: Record, K. E. / kereco01@email.uky.edu

93 **Abstract Title:** **The Cornea Donor Pool in 2030 - Where will my cornea come from?**

Author(s): PH Sheth, U of Kentucky
WS Van Meter, Department of Ophthalmology, U of Kentucky

Abstract:
Purpose: Donor demographics are applied to population projections 20 years in the future to theoretically examine the availability of corneas in 2030. Methods: Retrospective review of the EBAA Statistical Reports provide donor demographics and trends in tissue utilization dating back to 1991. US government data provide population projections for world, US, and individual states. Results: The number of corneas used in the United States has increased 33% since 2005 after being essentially flat from 1991 to 2004. At that utilization rate, the number of corneas needed in 2030 would increase 133% from current levels using the last 5 years data (66% using 10 year averaging, 46% using one year averaging). The population of the US will increase 17% and the world 20% during this interval, so population increase alone will not adequately cover projected tissue needs. Corneas were eliminated from surgical use in 2009 due to such factors as positive serology testing for hepatitis B (9%) and hepatitis C (3.8%), high risk features such as IV drug use noted on history or autopsy (17%), and slit lamp findings rendering the tissue unsuitable (25%). Social indicators suggest these adverse effects will become more important in the future. Yet the consent rate for corneal donations among suitable donors remains less than 20% in some states. Conclusion: The current utilization rate for corneal tissue will increase over the next 20 years and a number of adverse features will further shrink the donor pool. Increasing the donor consent rate is the most logical way to combat the potential dearth of useable corneal tissue by 2030.

Supported by: UK Center for Clinical and Translational Science
Primary Presenter / e-mail: Sheth, P.H. / preetisheth.uky@gmail.com
Mentor or Senior Author / e-mail: Van Meter, W. S. / wsvanmeter@aol.com

94 **Abstract Title:** **Changes in Nuclear Number and Myonuclear Domain Size with Aging**

Author(s): J.L.R. White, Div. of Physical Therapy, Dept. of Rehabilitation Sciences, College of Health Sciences, U of Kentucky
E. E. Dupont-Versteegden, Div. of Physical Therapy, Dept. of Rehabilitation Sciences, College of Health Sciences, U of Kentucky

Abstract:
Aging is associated with a loss of muscle mass and an increase in apoptosis in affected muscles. Therefore, we hypothesized that nuclear number would decrease and myonuclear domain would increase in rat soleus muscle in response to aging. Soleus muscles from 6, 15, 24 (n=6) and 32 (n=8) month old rats were collected and fixed in 4% paraformaldehyde for 48 hours. After fixation muscles were digested with 40% NaOH and single fibers were stained with DAPI. From each muscle at least 20 single fiber segments were photographed and nuclear number was determined in addition to nuclear domain by measuring the volume of the fibers. Nuclear number per volume was 1.9 fold higher in soleus from 32 compared to 6 month old rats while no difference was observed between 6, 15 and 24 months. There is a gradual decrease in myonuclear domain (cytoplasmic volume per unit DNA) from 6 to 15 (2%), from 15 to 24 (13%) and from 24 to 32 (31%) months of age which was only significant at the oldest age. Therefore, myonuclear domain is significantly lower in soleus muscle from 32 month old compared to all younger rats. In addition, no difference was observed in nuclear length. Contrary to our hypothesis, these data show that nuclear domain is smaller in aged animals, suggesting that there is a dysregulation between nuclear apoptosis and myonuclear domain.

Supported by: NIH award RO1AG028925
Primary Presenter / e-mail: White, J. / jena.white@uky.edu
Mentor or Senior Author / e-mail: Dupont-Versteegden, E. / eedupo2@uky.edu

95 **Abstract Title:** **The Effects of Aging and Altered Activity on Pax-7 Positive Satellite Cells and Cross Sectional Area of Soleus Muscle in Rats**

Author(s): J.M. Hoch, Department of Rehabilitation Sciences, College of Health Sciences, U of Kentucky
J. Mula, Departement of Rehabilitation Sciences, College of Health Sciences, U ok Kentucky
E.E. Dupont-Versteegden, Department of Rehabilitation Sciences, College of Health Sciences, U ok Kentucky

Abstract:
Introduction: Satellite cells are involved in the growth of muscle. Following disease or injury, satellite cells are activated to regenerate damaged muscle. In addition, following disease, injury or aging, muscle fibers atrophy significantly. The purpose of this study was to document changes in satellite cell number and muscle fiber cross sectional area (CSA) in both young and old rats, under three different conditions (controls(CON), hind limb suspended(HS), and hind limb suspended reloaded(HSRe)). Methods: A total of 60 rats (29 6months(MOS) and 31 32MOS) were randomly placed into three groups (CON, HS, and HSRE). Four 7μm sections of soleus for each of the groups were prepared for staining. Immunohistochemical staining was performed for each of the sections to determine the total number of PAX-7 positive satellite cells, and to measure CSA. A 2 x 3 ANOVA was employed to determine any interactions or main effects. LSD post-hoc analyses were used to explain significant interactions or main effects. The alpha value was set at 0.05. Results: PAX-7 staining was increased with age and decreased with hind limb suspension, while reloading restored expression in the young and old. Preliminary results indicate that CSA is decreased with age and hind limb suspension, and there is a trend for recovery with reloading for both ages. Conclusion: From these data we conclude that aged rats follow the same pattern of recovery from atrophy as young rats regarding satellite cell number and CSA in response to recovery after atrophy.

Supported by: NIH award: AG028925
Primary Presenter / e-mail: Hoch, J. M. / johanna.clark@uky.edu
Mentor or Senior Author / e-mail: Dupont- Versteegden, E. E. / eedupo2@email.uky.edu

96	Abstract Title:	**Concurrent Validity of Lysholm Scale Responses and Corresponding Performance Based Measures of Function in Articular Cartilage Patients**

Author(s): J. S. Howard, Department of Rehabilitation Sciences, College of Health Sciences, U of Kentucky
C. G. Mattacola, Department of Rehabilitation Sciences, College of Health Sciences, U of Kentucky
C. Lattermann, Department of Orthopaedics and Sports Medicine, U of Kentucky

Abstract:
Objective: To determine the validity of the 8 domains of the Lysholm relative to physical function. We hypothesized that the Lysholm domains would moderately correlate with walking, squatting, and stairs performance. Patients: 27 patients seeking treatment for knee articular cartilage defects. Methods: Preoperatively, all patients completed the Lysholm and assessment utilizing the Neurocom Long Forceplate (Clackamas, OR). Patients performed the Walk-Across, Squat, Sit-to-Stand, and Step-Up-and-Over. Spearman's rank correlations were used to determine the relationship between Lysholm domain (Limp, Support, Locking, Instability, Pain, Swelling, Stairs and Squatting) and performance variables. Results: Performance measures that correlated significantly to Limp were Walk-Across length (r=-.48), Squat at 30° (r=-.52), and Step-Up-and-Over uninvolved impact force (r=-.40). Support correlated to Walk-Across length (r=-.38) and speed (r=-.45); and Step-Up-and-Over uninvolved limb lift off force (r=-.42). Locking correlated to Step-Up-and-Over between limb time difference (r=.41). Instability correlated to Step-Up-and-Over uninvolved limb impact force (r=-.44). Pain correlated with Sit-to-Stand center of gravity sway velocity (r=.45); and Step-Up-and-Over uninvolved limb impact force (r=-.44). Swelling correlated to Walk-Across width (r=.47) and length (r=-.46); and Sit-to-Stand rise force (r=-.42). Stairs correlated to Walk-Across length (r=.40); Squat at 30° (r=-.44); Sit-to-Stand rise symmetry (r=-.49); and Step-Up-and-Over impact force on the uninvolved limb (r=-.41). Squatting correlated to Sit-to-Stand rise force (r=-.44). Conclusions: Moderate correlations exist between patient-reported and performance based measures of function. However, only 14-27% of the variability in self-reported function could be explained by performance. These results demonstrate the importance of collecting both patient-reported and performance based measures to evaluate functional capacity.

Supported by: UK Center for Clinical and Translational Science Seed Grant
Primary Presenter / e-mail: Howard, J. S. / j.s.howard@uky.edu
Mentor or Senior Author / e-mail: Mattacola, C. G. / carlmat@uky.edu

97	Abstract Title:	**Post operative alignment reults of computer assisted total knee arthroplasty in morbidly obese patients**

Author(s): P. Hosseinzadeh, Department of Orthopaedics, Marshall University School of Medicine
A. Oliashirazi, Department of Orthopedics, Marshall University Schoold of Medicine

Abstract:
Morbid obesity is defined as body mass index >40. Incidence of morbid obesity has increased in the United States from 2.9% of the population in 1994 to 4.7% in 2000.Obesity is associated with increased risk of osteoarthritis and other co morbidities including diabetes and hypertension.Increasing numbers of morbidly obese patients are seeking total knee arthroplasty.Limited literature is available about the results total knee arthroplasty in morbidly obese patients and available literature is retrospective with low number of patients.In a retrospective study with 5-14 year follow up of 39 morbidly obese patients after conventional knee arthroplasty, increase rate of revision and suboptimal alignment was reported. The methods that increase accuracy in total knee arthoplasty would be potentially beneficial in this group of patients. The Objective of this study was determine the postoperative alignment results after computer assisted total knee arthroplasty in this group of patients. Patients with BMI>40 who have undergone primary computer assisted total knee arthroplasty with a minimum of 2 year follow up were selected(107 patients).Surgeries have been perfomed between 4/2004-1/2007 by one surgeon using similar technique.Tibiofemoral angle was measured on the AP view of postoperative x-ray by one person 0-7 degrees of valgus was considered optimal alignment. Average postoperative alignment was measured as 3.7 degrees of valgus (range: 3 varus-7 valgus). Ninety seven percent of the measured alignments were in the optimal range. In conclusion computer assisted total knee arthroplasty is able to produce optimal postoperative alignment in patients with morbid obesity which could potentially improve long term clinical outcome.Future long term follow up studies are needed to compare this technique with conventional total knee arthroplasty in this group of patients.

Supported by:
Primary Presenter / e-mail: Hosseinzadeh, P. / hosseinzadeh@marshall.edu
Mentor or Senior Author / e-mail: Oliashirazi, A. / oliashirazi@marshall.edu

98 **Abstract Title:** **Defining the Three Dimensional Anatomical Footprints of the Brachialis, Biceps Brachii and Triceps Musculature.**

Author(s):
Y. N. Achuo-Egbe, U of Kentucky College of Medicine
M. Printz, U of Kentucky College of Medicine
A. Bachoura, M.D., Department of Orthopaedics, U of Kentucky
A. S. Deane, PhD, Department of Anatomy and Neurobiology
S. Kamineni, M.D., Department of Orthopaedics, U of Kentucky

Abstract:
Background: Little anatomical characterization of the distal insertions of the brachialis, biceps and triceps exists. Better anatomical understanding will lead to improvements in surgery. Aim: To define the precise footprints of brachialis, biceps and triceps using the FARO Arm 3D-Digitizer and Geomagic software. Method: 28 cadaveric arms were dissected leaving the distal insertions of brachialis, biceps, triceps and capsule. The FARO Arm (FARO, Lake Mary, FL) was utilized to scan the surface of the elbow. The FARO probe was then utilized to trace the footprints of the muscles. The elbow was disarticulated, and the bare bones were individually scanned. The scans were analyzed using Geomagic Qualify 11, 12(Geomagic, Research Triangle Park, NC) enabling accurate analysis of insertional surface area, length and width. Results: The triceps area was significantly greater (421.1 ± 221 mm2) than brachialis (223.3 ± 152 mm2) and biceps (188.6 ± 155 mm2). The triceps width was insignificantly greater (18.9 ± 10 mm) than brachialis (11.2 ± 5 mm) and biceps (9.1 ± 6 mm). However, there was no significant difference between the length of triceps (32.9 ± 14 mm) brachialis (27.6 ± 12 mm) and biceps (24.4 ± 9 mm). Conclusions: This is the first study to demonstrate differences in the areas, lengths and widths of biceps, brachialis and triceps insertions. The muscle footprint shape significantly affects the surface area while maintaining length and width. The hardware and software used introduced unforeseen errors, which include inability to compensate for the probe and manual alignment of scanned images.

Supported by: Elbow Shoulder Research Center, Department of Orthopaedics, University of Kentucky and Professional Student Mentored Research Fellowship (PSMRF) Scholarship

Primary Presenter / e-mail: Achuo-Egbe, Y. N. / egbeyvette@uky.edu
Mentor or Senior Author / e-mail: Kamineni, S. / srinath.kamineni@uky.edu

99 **Abstract Title:** **Multivariate Exploration of Time to Boundary Outcomes of Chronic Ankle Instability**

Author(s):
C. P. Starnes, Department of Biostatistics, U of Kentucky
H. M. Bush, PhD, Department of Biostatistics, U of Kentucky
P. O. McKeon, PhD, ATC, Department of Rehabilitation Sciences, U of Kentucky

Abstract:
Chronic ankle instability (CAI) is a condition associated with long term recurrent ankle dysfunction subsequent to an initial sprain. Postural control deficits have been identified as contributing factors to this condition, but it is unclear whether these deficits can be detected with laboratory- and clinician-oriented measures. Postural control variables are highly correlated, and investigations are often difficult given the number of correlated variables to consider. Data reduction through multivariate methods allow for investigating relationships with many correlated variables. Using data collected on CAI (n=16) and matched healthy subjects (n = 16) multivariate methods were used to determine the combination of postural control variables that best identified impaired postural control in those with CAI. Data reduction indicates that >90% of the variability in the data can be explained by 3 component variables which are weighted linear combinations of 12 original TTB postural control variables. Those postural control variables with the greatest weights were those that measure TTB changes in the anteroposterior (AP) direction with eyes open. This could indicate that due to a more constrained sensorimotor system in those with CAI; these subjects had less time to make corrections in order to maintain single limb stance. The specific deficits in the AP direction are consistent with what has been reported in the literature previously and may be associated with a reweighting of somatosensory information due to altered sensory information from damaged ankle joint receptors.

Primary Presenter / e-mail: Starnes, C. P. / catherine.starnes@uky.edu
Mentor or Senior Author / e-mail: Bush, H. M. / heather.bush@uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

100	Abstract Title:	**Faculty Evaluation of Anesthesiology Residents: Resident Satisfaction and Faculty Promotion is More Important Than Quality Constructive Formative Feedback**

Author(s):
J. Reynolds, College of Medicine, U of Kentucky
R. Schell, Department of Anesthesiology, U of Kentucky
A. DiLorenzo, Department of Anesthesiology, U of Kentucky
R. Fragneto, Department of Anesthesiology, U of Kentucky
K. Hatton, Department of Anesthesiology, U of Kentucky
E. Bowe, Department of Anesthesiology, U of Kentucky

Abstract:

Introduction: Previous research has demonstrated that students' satisfaction with feedback does not correlate with the quality of the feedback but is dependent instead on affirmation1. In addition, faculty members are aware of which comments will be perceived as negative or positive by residents2. The purpose of this study was to investigate the various reasons that may lead to faculty avoiding giving constructive feedback that may be perceived as negative. Methods: After IRB approval of the study, Department of Anesthesia Faculty received an email explaining the study and a link to the survey. They indicated consent to participate in the study by clicking on the link and completing the survey. Forty-three completed the survey (91% response rate). A 5-point Likert scale was used. Results: The survey results (Table) show that faculty acknowledge the value of giving constructive feedback to residents and yet often avoid giving it. They admit they are more honest in anonymous evaluations. Given the lack of anonymity in formative and summative evaluations administered by this Department, the most common reason for avoiding giving negative feedback was fear of damaging the faculty/resident relationship. Faculty is also afraid of how retaliation from residents may affect their potential for promotions and tenure. For these reasons, the majority of faculty (69%) indicated that evaluations of residents should be done anonymously. Discussion: The full potential of the educational process is being hindered when honest, constructive feedback is not given to resident learners. The faculty is aware of which statements will be perceived as negative by residents and are avoiding these statements. For various reasons they are choosing to try to preserve the satisfaction of the residents rather than providing meaningful, quality feedback that could potentially be perceived as negative. In an attempt to maintain resident's satisfaction, faculty may encounter less relationship problems, less retaliation, and maintain better prospects for future promotion but at the same time they may be sacrificing quality feedback for the residents. More research is needed to analyze these trends in additional departments, colleges, and universities.

Primary Presenter / e-mail:	Reynolds, J. / jrre222@uky.edu
Mentor or Senior Author / e-mail:	Schell, R. / rmsche3@email.uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

101	**Abstract Title:**	**First Impression during the Residency Interview Correlates with the Final Rank List Position**

Author(s):
J. R. Reynolds, College of Medicine, U of Kentucky
R. Fragneto, Department of Anesthesiology, U of Kentucky
R. Schell, Department of Anesthesiology, U of Kentucky
A. DiLorenzo, Department of Anesthesiology, U of Kentucky
H. Li, Department of Epidemiology & Biostatistics, U of Kentucky
E. A. Bowe, Department of Anesthesiology, U of Kentucky

Abstract:

Introduction: Decisions to interview residency candidates are often based upon factors such as USMLE scores and medical school performance. The interview is a more subjective aspect of the selection process. The book, Blink: The Power of Thinking Without Thinking, describes the concept of the ability to discern important information about a person within just a few seconds. Our interview team utilizes this concept and attempted to correlate it with other selection factors and outcomes. Methods: Deidentified data from 430 applicants (three years; 2007-10) were analyzed. Each applicant was interviewed by the same four faculty and one resident and assigned a "Blink"□ score - a score assigned and recorded within the first 30 seconds of the interview where 1= not an appropriate candidate, 5= excellent candidate. Excluded from the study were applicants who were students of our medical school or who did a rotation in our department as a Blink score cannot be assigned to someone already known by the interviewer. Spearman's correlation coefficients were determined for mean Blink score and final applicant position on the NRMP rank list, mean overall faculty score for applicant based on application and interview, applicant USMLE scores, mean score for review of ERAS materials, and mean applicant scores for structured interview questions based on the general competencies. Correlation between the overall score assigned by the resident interviewer and rank list order was also determined. A mean Blink score was determined for each gender and compared using the t test. Multiple regression analysis was utilized. Results: Using Spearman's rank correlation coefficient, significant correlations were found between the Blink score and overall faculty score, rank list position, scores for structured interview questions, review of ERAS score, and Step 2 score (Table 1). Among all the variables the best predictors of rank list position according to multiple regression analysis were overall faculty score, ERAS score, interpersonal and communication skills score, overall resident score and gender. The mean Blink score for male and female was 3.5 and 3.8 respectively ($p<0.0001$). Discussion: The snap judgments made by the interview team (Blink score) correlated significantly with rank list position and the following scores: overall faculty score, structured interview questions, review of ERAS materials, and Step 2. Despite the Blink score correlating well with these variables, it was not among the best predictors of rank list position. Whether "Blink"□ assessment correlates with resident performance outcomes has yet to be studied. References: Gladwell, Malcom.(2005) Blink:The Power of Thinking Without Thinking.

Primary Presenter / e-mail: Reynolds, J. / jrre222@uky.edu
Mentor or Senior Author / e-mail: Schell, R. / rmsche3@email.uky.edu

102	**Abstract Title:**	**Utilization of Internet Resources Regarding Anesthesia and Surgical Procedures in Caregivers of Pediatric Surgery Patients**

Author(s):
C.J. Koons, College of Medicine, U of Kentucky
A.M. Reddy, Department of Anesthesiology, U of Kentucky

Abstract:

Purpose: To asses the utilization of internet resources by caregivers about anesthesia and surgical procedures before surgery. Background: Parents and patients alike are often anxious about what will go on once they are in the operating suite, nowhere is this more apparent than in the pediatric patient population. Many institutions across the country, in an effort to be more patient centered, have developed materials for providing patients and families with information about their planned surgical procedures and anesthesia care. Methodology: 95 parents and caregivers randomly and voluntarily participated in a survey during the pre-operative period. The survey collected demographics and information pertaining to use of internet websites in obtaining information. Results: Many caregivers (43.6%) use the internet as their primary source of for obtaining information about anesthesia and operative procedures. Over half of respondents (52.6%) used forums, blogs, or Wikipedia as their primary source. Many of these resources may be biased, are not peer reviewed and are representative of the opinions of individuals. Conclusions: Data suggests that most patients and families would benefit from an internet accessible resource constructed by their healthcare team with accurate information regarding planned anesthesia and surgical procedures. Providing this resource early would alleviate caregiver fears and abrogate the need to seek information from resources of potentially dubious origin.

Supported by: UK Department of Anesthesiology

Primary Presenter / e-mail: Koons, C. J. / curtiskoons@uky.edu
Mentor or Senior Author / e-mail: Reddy, A. M. / aredd2@email.uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

103 **Abstract Title: Improving Health Literacy through Rural Journalism**

Author(s): A. Cross, Institute for Rural Journalism and Community Issues, U of Kentucky

Abstract:

An extension program in a journalism school has developed strategies and tactics for improving coverage of health care and health issues in rural newspapers, especially in Appalachia. Special health sections for weekly Appalachian newspapers were produced with foundation and advertiser support and mailed to non-subscribers, who said they would be more likely to subscribe if the newspaper included such information regularly. The sections, and local health data provided by the program, encouraged other newspapers in Kentucky to produce their own sections. Seminars for rural journalists provided assistance in covering health issues, including tobacco-related issues and diabetes. Recruitment strategy and tactics for the latter seminar, personal letters to counties with high rates of diabetes, proved highly productive. Preliminary research on health coverage in Kentucky newspapers, which is continuing, found that a plurality of articles about health behavior in one region were advertorial or otherwise not properly sourced, and that few newspapers used articles generated by College of Medicine and university public-relations office about regional health issues. Better results are being seen with Kentucky Health News Service, which is providing original stories and localized data to newspapers, and blogging excerpts of stories from other sources, to inform health journalism and improve health literacy.

Supported by: Foundation for a Healthy Kentucky grant/contract

Primary Presenter / e-mail: Cross, A. / al.cross@uky.edu
Mentor or Senior Author / e-mail: Cross, A. / al.cross@uky.edu

104 **Abstract Title: How Adolescents Manage Their Asthma: A Focus Group Study**

Author(s): R. Lefevre, College of Medicine, U of Kentucky
M. Love, Department of Family and Community Medicine, U of Kentucky
V. Holiday, College of Medicine, U of Kentucky

Abstract:

CONTEXT: Little is known about the physician-patient relationship between adolescents that have been diagnosed with asthma and their primary asthma care provider. OBJECTIVE: To describe what adolescents with asthma value in the care provided for their asthma. HUMAN SUBJECTS REVIEW: IRB approved, expedited review. DESIGN: Descriptive study. Initial one on one interviews with adolescents to identify potential topics followed by focus groups with about six to eight adolescents to encourage discussion. In addition to the discussion groups, all participants will be asked to complete a survey about their asthma care. SETTING: General community of Lexington, Kentucky. PARTICIPANTS: Adolescents currently in high school that have been diagnosed with asthma. It is expected that six to eight focus groups will be necessary to identify all potential themes. Participants recruited through flyers in the local community. ANTICIPATED RESULTS: First initial interview indicates that continuity of care with physician is an important factor in the physician patient relationship. Other factors include perceived access to care and education provided during care. CONCLUSIONS: As adolescents make the transition from childhood to adulthood, the responsibility of asthma care transfers to the adolescents' shoulders. Identifying the aspects of care valued by adolescents could potentially improve the delivery of care by physicians.

Supported by: Family and Community Medicine, U of Kentucky

Primary Presenter / e-mail: Lefevre, R. / ryan.lefevre@uky.edu
Mentor or Senior Author / e-mail: Love, M / mlove@email.uky.edu

105 **Abstract Title: The Value of Mediastinoscopy in the Management of Thoracic Disease**

Author(s): N. Borges, MS III, University of Kentucky College of Medicine
S. P. Saha, MD, MBA, Division of Cardiothoracic Surgery, U of Kentucky

Abstract:
Background: Mediastinoscopy is a commonly used method in the diagnostic evaluation of diseases of the chest. Since its introduction by Carlens in 1959, it has been established as one of the gold standard techniques for the evaluation of thoracic disease, especially lung cancer. Recent reports indicate that this method is underutilized in the community practice. Objectives: The purpose of this study is to analyze the morbidity, mortality and accuracy of mediastinoscopy in the diagnosis of thoracic disease at our academic medical center. Materials and Methods: We performed a retrospective chart review of 287 patients at the University of Kentucky Chandler Hospital who had mediastinoscopy between 2004 and 2009. Of the 287 patients selected for this study, 57% were males and 43% females. The average age of the patients was 63 years with 234 patients being between 50 and 80 years old. One hundred and ninety eight patients were diagnosed with cancer, while 89 had non-malignant diseases. Of the 198 patients diagnosed with cancer, 107 had metastatic disease, 65 of which were diagnosed with mediastinoscopy, while the remaining 42 patients required further diagnostic procedures. Results: The complication rate was only 0.014% with 4 patients having complications. Conclusion: Mediastinoscopy is a safe and effective procedure in the diagnosis and management of thoracic disease.

Supported by: Division of Cardiothoracic Surgery
Primary Presenter / e-mail: Borges, N. / nyalborges@uky.edu
Mentor or Senior Author / e-mail: Saha, S. / ssaha2@email.uky.edu

106 **Abstract Title: The Use of Supplemented Dextrose Infusion in Medically Critically Ill Adult Patients**

Author(s): S. R. Peters, Department of Pharmacy U of Kentucky
A. M. Cook, Department of Pharmacy U of Kentucky
B. Magnuson, Department of Pharmacy U of Kentucky
P. S. Winstead, Department of Pharmacy U of Kentucky

Abstract:
Purpose: Early nutritional support is imperative to fulfill the increased metabolic needs associated with acute illness, with enteral nutrition as the recommended route. Enteral nutrition (EN) is preferred over parenteral nutrition (PN) based on data suggesting decreased morbidity and mortality. At our institution one option for patients unable to receive EN acutely is to administer a daily supplemented dextrose infusion composed of 10% dextrose, multivitamins and trace elements. The primary outcome of this study is to evaluate time to initiation of EN in patients that received the supplemented dextrose infusion compared to those who did not. Several secondary objectives will be evaluated to aid in characterizing the use of the supplemented dextrose infusion at our institution. Methods: This was a retrospective, cohort chart review conducted at a tertiary teaching institution. Medically critically ill patients requiring mechanical ventilation were included if predefined inclusion and exclusion criteria were met. Patients receiving the supplemented dextrose infusion were matched in a 1:1 fashion, via propensity score, with patients who did not. Baseline characteristics were compared using Student unpaired t test or Wilcoxon Rank Sum Test in the case of continuous variables and chi-square test in the case of dichotomous variables. Cox proportional hazard regression was performed to analyze the primary objective. Hazard ratios were computed from the coefficients in Cox Proportional model and 95% confidence intervals were calculated for all the variables. Results: Data collection in progress, results to be presented. Conclusions: It is anticipated that this project will demonstrate inconsistencies in prescribing and administration patterns of supplemented dextrose infusion within the institution. It is expected that the use of supplemented dextrose infusion will not delay time to initiation of enteral nutrition.

Primary Presenter / e-mail: Peters, S. R. / spe225@email.uky.edu
Mentor or Senior Author / e-mail: Winstead, P. S. / p.shane@uky.edu

107 **Abstract Title: Risk Factors Associated with Thrombocytopenia in the Intensive Care Unit Population**

Author(s): J. W. Craig, Department of Pharmacy Services, U of Kentucky
A. M. Cook, Department of Pharmacy Services, U of Kentucky
S. P. Winstead, Department of Pharmacy Services, U of Kentucky

Abstract:

Purpose: Thrombocytopenia is commonly observed in critically ill patients and establishing a definitive cause may be difficult. Risk factors associated with this population include specific disease states, invasive catheters, and administration of multiple medications believed to cause thrombocytopenia. It is associated with prolonged hospital stays and overall worse outcomes for critically ill patients. The purpose of this study was to identify critically ill patients with thrombocytopenia defined as a platelet count of < 150,000 and evaluate common factors in this population that may contribute to this clinical finding. Methods: This was a retrospective, medical record review of patients admitted to all adult ICU's at a 473-bed academic, tertiary-care medical center. Eligible patients included those with an ICU length of stay of at least 4 days and administration of one of the following medications: H2-receptor antagonists, proton pump inhibitors, vancomycin, linezolid, unfractionated heparin, and/or low-molecular weight heparin. Patients were excluded from the study if they were transplant recipients, cirrhotic, had known malignancy, had cardiothoracic surgery, were transferred from an outside hospital, and/or received platelet transfusion within 24 hours of admission. Patients were stratified into two categories based on the presence or absence of a diagnosis of thrombocytopenia. The primary objective of the study was to determine the relationship of various factors with the development of thrombocytopenia. Secondary objectives included determining the rate of thrombocytopenia and analyzing the cost-effectiveness of using agents with presumed lower thrombocytopenia risk. A multivariate analysis of disease states, medications, and severity of illness was performed to determine a relationship between the specified parameters and thrombocytopenia. Results/Conclusion: Data collection is in progress.

Primary Presenter / e-mail: Craig, J. W. / jamie.w.craig@uky.edu
Mentor or Senior Author / e-mail: Cook, A. M. / amcook0@email.uky.edu

108 **Abstract Title: Risk factors for venous thromboembolism in patients with cirrhosis**

Author(s): K.A. Walsh, Department of Pharmacy, UK HealthCare
D.A. Lewis, Department of Pharmacy, UK HealthCare
T.M. Clifford, Department of Pharmacy, UK HealthCare
J.C. Hundley, Department of Surgery, UK HealthCare
G.A. Davis Department of Pharmacy, UK HealthCare

Abstract:

Purpose: Venous thromboembolism (VTE) prophylaxis in patients with cirrhosis presents a unique challenge due to complications associated with the disease, including esophageal varices, thrombocytopenia and elevated international normalized ratios (INR). When evaluating whether these patients require VTE prophylaxis upon hospitalization, practitioners must weigh the risk of bleeding, and their perceived 'auto-anticoagulation', against the risk of developing VTE. Therefore, it would be advantageous if risk factors for the development of VTE in this population were identified. This study was designed to identify risk factors associated with the development of VTE in cirrhotic patients. Methods: This study is a retrospective, case control study. Patients at the University of Kentucky Chandler Hospital with a diagnosis of cirrhosis and VTE from October 2006 to July 2010 were matched in a 1:3 fashion with cirrhotic patients who did not develop VTE. The primary objective was to determine if there were significant differences in laboratory values between the two groups. Secondary objectives include examining the relationship between VTE incidence and INR. Results: Twenty seven patients with cirrhosis during this time period were diagnosed with VTE. Preliminary results indicate that aspartate aminotransferase (AST), alanine transaminase (ALT), albumin, and hematocrit were significantly lower in cirrhotic patients with VTE, compared to those who did not develop VTE. In addition, there does not appear to be a correlation between VTE incidence and INR.

Primary Presenter / e-mail: Walsh, K. A. / kwa225@uky.edu
Mentor or Senior Author / e-mail: Davis, G. A. / gadavi00@uky.edu

109	Abstract Title:	**The Endoscopic Component Separation Technique for Hernia Repair Results in Reduced Morbidity Compared to the Open Component Separation Technique**

Author(s):
M. Guirguis, Department of Surgery, University of Kentucky
L. E. Bendure, College of Medicine, University of Kentucky
D. L. Davenport, Department of Surgery, University of Kentucky
J. S. Roth, Department of Surgery, University of Kentucky

Abstract:
INTRODUCTION: The component separation technique for hernia repair results in significant wound morbidity due to the need for large undermining skin flaps. The endoscopic component separation technique allows for advancement of the abdominal wall while preserving the blood supply originating from the epigastric vessels. This study compares the outcomes following hernia repair utilizing these techniques. METHODS: A retrospective review of patients undergoing component separation or endoscopic component separation hernia repair from 2008-2010. Patients underwent open component separation or endoscopic component separation with closure of the linea alba and reinforcement with mesh. RESULTS: Thirty five patients were identified that underwent a component separation (15 open component separation [CST] and 20 endoscopic component separation [ECST]. There was no difference in hospital length of stay (CST 5.2±3.2 d vs. ECST 6.2±3.6 d, p=0.74) or operating room times (CST; 251±70 min vs. ECST; 234±55 min, p=.39). Wound complications occurred in 60% of CST and 20% of ECST, p=0.04. One recurrent hernia was identified in the CST group with a mean follow up of 8 months (range 1-21 mos). No recurrences were seen in the ECST group. CONCLUSION(S): ECST is associated with comparable hospital length of stay and operative times and reduced wound complications compared to CST.

Supported by: Professional Student Mentored Research Fellowship University of Kentucky
Primary Presenter / e-mail: Bendure, L. / lebend2@uky.edu
Mentor or Senior Author / e-mail: Roth, J. S. / s.roth@uky.edu

110	Abstract Title:	**Development of Impedance Spectroscopy as a Means of Evaluating Skin Barrier Function and Micropore Formation Following Microneedle Treatment in Human Subjects**

Author(s):
N. K. Brogden, Department of Pharmaceutical Sciences, University of Kentucky
L. J. Crofford, Department of Internal Medicine, University of Kentucky
A. L. Stinchcomb, Department of Pharmaceutical Sciences, University of Kentucky

Abstract:
Hypothesis: Microneedle (MN) - enhanced transdermal delivery allows drugs to be delivered systemically via micropores formed in the stratum corneum (the outermost layer of the skin), which serves as the skin's primary barrier. Electrical impedance provides important information regarding the skin's barrier function, but impedance methods have not been formally investigated for evaluating pore formation following MN treatment. The objective of this work was to develop an impedance spectroscopy technique for evaluating pore formation following MN treatment in human subjects. Methods: Six sites on the upper arms of subjects were treated with MN arrays. Three sites were evaluated with Ag/AgCl dry electrodes; the other 3 with gel electrodes. Repeated measurements were made using either light pressure to hold the electrode to the skin, or direct pressure (applied by the thumb of the investigator). ANOVAs, t-tests, and descriptive statistics were used for data analysis. Results: Ten subjects completed the protocol (4 males, 6 females, average age of 27 ± 4.1 years). Mean impedance values dropped significantly from baseline to post-MN for the majority of sites, irrespective of pressure or electrode type ($p < 0.05$). Measurements with gel electrodes were generally lower and more stable (both light and direct pressure techniques) for intact and post-MN treated skin. Overall variability was also lower with gel electrodes, particularly for post-MN measurements. Conclusion: Impedance spectroscopy was an effective technique for evaluating micropore formation following MN treatment. Gel electrodes applied with direct pressure were superior, introducing less variability and fluctuation between sites and measurements.

Supported by: NIH award: F31DA029374 UK Clinical and Translational Science seed grant
Primary Presenter / e-mail: Brogden, N. K. / nkbrog2@email.uky.edu
Mentor or Senior Author / e-mail: Stinchcomb, A.L. / astin2@email.uky.edu

Poster Presentation Abstracts
6th Annual CCTS Spring Conference
Appalachian Health Summit: Focus on Obesity
April 21, 2011

111	**Abstract Title:**	**Implementation of a septic shock order set and resuscitation protocol at a tertiary medical center**

Author(s):
M. Nestor, PharmD, Department of Pharmacy Services, U of Kentucky
K. Hatton, MD, Department of Anesthesiology, U of Kentucky
P. Branson, MSN, U of Kentucky
J. Flynn, PharmD, Department of Pharmacy Services, U of Kentucky

Abstract:

Septic shock is a serious medical condition characterized by the presence of hypotension not responsive to fluid resuscitation in the setting of the traditional sepsis criteria. These patients require multiple, complex interventions for treatment are aimed at the causative infectious agent, the restoration of appropriate hemodynamics, and to prevent further organ injury. Consensus guidelines for the management of patients with septic shock have established specific process measures to restore hemodynamic targets, to identify the infectious source, and to initiate the treatment of the underlying infectious processes. With the goal of improving the care of patients with septic shock, a computer-based order set was developed to order blood, urine and respiratory cultures, initial empiric antibiotics, fluid boluses for resuscitation and conditional orders for vasopressor and inotropic support. This order set was also developed to initiate a paging system alert to a specific team of clinical pharmacy staff, critical care nurses, and materials management services for their additional assistance in the management of patients with septic shock. The primary role of the pharmacist responding to these alerts is to assist in the initial selection and administration of empiric antibiotics, the evaluation for the appropriateness of corticosteroid and drotrecogin alfa administration, and the management of other drug and drug product issues during the early resuscitative period. A septic shock response cart was designed to complement the order set as well. The cart contains initial doses of antibiotics, fluids, vasopressor and inotrope products, materials for placement of intravenous access, and materials for laboratory samples to be utilized in early resuscitation efforts. Adult patients that are resuscitated with the septic shock order set from 1 September 2010 will be identified and compared to a historical control group of patients with diagnosis related group codes for severe sepsis or septic shock. The primary endpoint will be to evaluate the time to the first dose of antibiotic administration compared to historical controls. The secondary endpoints will evaluate mortality, intensive care unit and hospital length of stay, the appropriateness of the initial antibiotic therapy, and the number of ventilator days. At present, patient enrollment in the septic shock group, data collection, and analysis is ongoing.

Primary Presenter / e-mail:	Nestor, M. / mne223@uky.edu
Mentor or Senior Author / e-mail:	Flynn, J. / jeremy.flynn@uky.edu