Current FAMEPRO Projects (2018-2019)

The aim of this initiative is to provide guidance and support to faculty members to conduct and complete clinical research projects and to prepare and disseminate results through clinical scholarship.

Our 2018-19 participants and projects are listed below.

Retrospective Chart Review of Emergency Department Patients with Cancer and Non-Neutropenic Fever

PI: Jason Bischof, MD
Mentor: Jeffrey Caterino, MD

Increasingly, acute care for cancer patients is occurring in emergency departments (ED). An estimated 4.5 million such visits occur yearly. Observational data reveals that approximately 60% of these patient visits result in an admission. Many of these ED visits are in the setting of a febrile illness. Unfortunately, the current literature provides limited guidance on how to treat such patients. Guidance exists in the setting of a neutropenic fever; however, no such protocols exist for patients with non-neutropenic fever, the majority of patient visits with fever. This project aims to characterize the patient population with cancer presenting to the OSUWMC ED with non-neutropenic fevers in hopes of identifying key clinical characteristics that would allow for the risk stratification of these patients. We hypothesize that a great number of these patients who are currently being admitted may be able to be safely treated with close outpatient follow up or with a short observation stay. This would provide significant benefits to patients and the medical system by reducing the number of admissions, reducing costs of care associated with admission, and improving patient experience and quality of care by identifying unnecessary admissions. A retrospective chart review will be conducted of 300 patients with active cancer (James patient within the past year) presenting to the OSUWMC ED with a chief complaint of fever or a documented fever within the first 6 hours of the ED visit. Patients will be identified by querying the OSUWMC information warehouse. Exclusion criteria will include corrections patient, neutropenic patients, pregnant patients, and trauma patients. As a result of the methodology, minimal risk exists to subjects.

Clinicopathologic Correlation of Graft-versus-Host Disease in the Pediatric Population

PI: Miriam Conces, MD
Mentor: Shamlal Mangray, MBBS

Acute graft-versus-host disease (GVHD) remains a significant cause of morbidity and mortality after allogeneic hematopoietic stem cell transplant (HCT). After transplant, 30-50% of patients develop GVHD and up to 15% are clinically severe. At onset, the gastrointestinal tract is involved in approximately half of all cases, but clinical symptoms can be relatively nonspecific and include nausea, decreased appetite, vomiting and diarrhea. In a stem cell transplant recipient, causes such as drug toxicity, engraftment syndrome and infections can closely mimic symptoms of GVHD. Therefore, the clinical diagnosis of GVHD often requires diagnostic biopsies for confirmation. In conjunction with clinical data, this study will retrospectively review all gastrointestinal biopsies obtained from HCT patients for a 10 year period (2007-2017). The histologic features of the biopsies will be compared to the clinical characteristics of these patients. Immunohistochemistry, an ancillary diagnostic technique, will be used to highlight neuroendocrine cells in the biopsies that may be affected by GVHD. Minimal risk is associated with this study since all included biopsies are from archived tissue taken for clinical care purposes. The results will provide further insight into the pathologic features that may help to differentiate GVHD from histologic mimics.
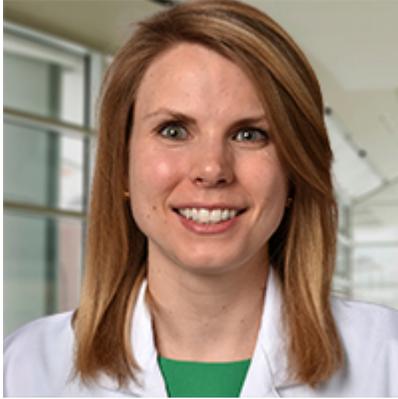
Clinical utility of bronchoalveolar lavage in alveolar hemorrhage

PI: Lynn Fussner, MD
Mentor: Mark Wewers, MD

Alveolar hemorrhage (AH) is a life-threatening clinical syndrome associated with both immune and non-immune mediated etiologies. It is typically diagnosed using bronchoalveolar lavage (BAL), a diagnostic procedure performed via bronchoscopy to sample alveolar cells and proteins. With current techniques, BAL can identify the presence of blood in alveoli, but not why it is there. This is problematic as management of the varying etiologies of AH is often mutually exclusive, with significant risk of harm if misdirected. It is suspected that BAL fluid contains more specific information, including markers to differentiate among AH etiologies. Future study in this area will involve direct analysis of BAL fluid across diagnoses. The first step, however, is to identify the type and frequency of clinical scenarios in which AH occurs, and to define the current status of available clinical data for this issue. We will perform a retrospective chart review of OSUWMC patients diagnosed with AH from 2007-2017. Initial search terms will utilize Provation (bronchoscopy documentation software) and Information Warehouse. Bronchoscopy reports will then be screened to ensure BAL description is consistent with AH, identifying patients appropriate for inclusion. Clinical data will be abstracted from IHIS, including symptoms, laboratory and BAL results, imaging, respiratory status, therapies employed as a result of BAL, and diagnoses for the episode of care. Data will be collected using REDCap, and analyzed using JMP. There is no anticipated harm to subjects with this retrospective analysis. The benefits are important as there has been little change in our diagnostic tools for AH in several decades. This work has the potential to change how AH is diagnosed, improving management and outcomes.

Understanding Obesity Risk in the first 1000 days in low-income populations

PI: Amrick Singh Khalsa, MD
Mentors: Alex Kemper, MD and Kelly Kelleher, MD, MPH

Childhood obesity continues to be a major health concern for the United States, with high prevalence in low-income (Rogers 2015) and minority populations (Ogden 2014). Sociodemographic disparities in obesity are noted within the first 1000 days (conception to age 2 years, Ogden 2014). However, clinicians are not provided much guidance in identifying obesity in this vulnerable age group. The overall objective with this proposal is to identify clinical thresholds and sociodemographic predictors of obesity within the first year of life that predicts obesity at age 4 years, in a low-income urban population. We will conduct a retrospective data analysis of an existing longitudinal cohort of low-income families. Through this existing cohort, we have anthropometric data available for an average of 13 visits/child for nearly 33,000 children (full-term) who were seen for well-child visits through the Nationwide Children's Hospital primary care clinics. Additionally, we have the ability to conduct several subgroup analysis of major sociodemographic and maternal characteristics including age, race, maternal education, marital status, maternal pre-pregnancy BMI, maternal diabetes, maternal smoking during pregnancy. The PI has access to existing data analysts and a biostatistician who are versed with the data and will be available to aid in the analysis. As the data for this project is already collected and de-identified, the risk to the child/family is minimal. This pilot data will potentially provide preliminary evidence that clinicians can use to screen and identify children at risk of obesity in early childhood. This will also serve as pilot data in the PI's career development application to further understand modifiable risk factors of obesity in the first 1000 days.

Nutritional Deficiencies in Myotonic Dystrophy type 1

PI: Samantha LoRusso, MD
Mentor: David (William) Arnold, MD

The goal of this study is to investigate nutritional status in patients with myotonic dystrophy type 1 (DM1) and to determine whether patients with DM1 are more likely to experience deficiencies compared to other forms of muscular dystrophy. This prospective study will evaluate nutritional status by collecting serum samples from patients with muscular dystrophy measuring various vitamins, minerals, hormones, and cholesterol levels. Patients will also fill out questionnaires assessing diet, lifestyle, social support, gastrointestinal symptoms, cognitive status, fatigue, and quality of life. In addition, each patient's medical chart will be retrospectively reviewed to obtain basic demographics, genetic results, medical and surgical history, medications, EMG findings, PFT results, and swallow study results. We hope to enroll at least 25 DM1 patients and 40 patients with other muscular dystrophies. The main risks to the patients include the risk associated with blood draws which are minimal (discomfort). In addition, there is the risk associated with collection of private health information (PHI) and the loss of patient confidentiality; however, patient identifiers will be kept in a REDCap database. The primary potential benefit of this research for the individual patient is identification of a treatable nutritional deficiency. The benefit to the medical community is greater understanding of nutritional status in patients with myotonic dystrophy that could result in a change in disease monitoring and standard of care.

Characterizing kidney disease associated variant APOL1 specific proteomic networks in focal segmental glomerulosclerosis

PI: Sethu Madhavan, MBBS
Mentor: Brad Rovin, MD

Chronic kidney disease (CKD) is significantly common in African Americans and are four times more likely than white patients to progress to end stage renal disease. Variants in apolipoprotein L1 (APOL1) gene associates with increased risk of CKD including hypertension-related CKD and focal segmental glomerulosclerosis (FSGS) in individuals with African ancestry. FSGS involves progressive scarring of glomeruli of the kidney where APOL1 protein is expressed. So far, physiological function or mechanisms by which APOL1 variants contribute to the pathogenesis of CKD remain unclear. Project design and procedures: Archived frozen human kidney biopsies with a diagnosis of FSGS and will be obtained from Department of Pathology. After determining the APOL1 genotype in the biopsy tissue, will select 3 samples without kidney disease associated APOL1 variants and 3 samples with homozygous APOL1 variants for this study. Glomeruli will be isolated by laser capture microdissection in collaboration with Department of Pathology. Proteomics studies will be performed at the Mass Spectrometry and Proteomics facility at OSU. Data analysis will be performed by the applicant. Risks: We are collecting archived kidney biopsy specimens which were originally obtained for non-research purposes. An IRB application to collect these tissues is currently under review. No protected health information will be collected and this study involves no more than minimal risk to the participants. Anticipated benefits and importance of knowledge: These studies will provide important information that will help understand the role of APOL1 in normal kidney function and will provide novel information on how to approach variant APOL1 function with therapeutic strategies.

To Evaluate the Role of Plasma Catecholamine Levels in Predicting the Development of Myocardial Depression in Acute Neurological Patients

PI: Shraddha Mainali, MD
Mentor: Ayesha Hasan, MD and Barbara Rogers, MD

Takotsubo syndrome (TTS) is a reversible heart failure (HF) syndrome caused by acute surge of endogenous or exogenous catecholamines. The pathophysiology of TTS is well understood and the myocardial depression (MD) is thought to be multifactorial. TTS is known to predominantly occur in postmenopausal women (~90%). Elderly are more likely to be affected (90% are >50 yrs). In this study, we will investigate the level of plasma catecholamines, associated with MD as noted on Transthoracic ECHO (TTE) by evidence of regional wall motion abnormalities (RWMA) with or without HF. TTS is commonly diagnosed after the onset of HF but we hope to identify patients during the period of early MD. Identification of early MD changes can lead to alteration of management strategies to prevent HF. Highly selected patients with Subarachnoid Hemorrhage (SAH) and Acute Ischemic Stroke (AIS) requiring induced hypertension with the use of norepinephrine infusion will be involve in this pilot study. Given the prevalence of TTS on females and elderly, we will study 10 female patients >50 years admitted to the neuro ICU with diagnosis of either AIS or SAH. Only patients predicted to be on norepinephrine infusion for at least 48 hrs will be selected. Patients with history of coronary artery disease, smoking, poorly controlled diabetes with HbA1c >8 and uncontrolled hypertension will be excluded. Baseline plasma catecholamine levels, TTE, Troponin T, EKG and BNP will be obtained. Thereafter, we will follow daily labs, EKGs and TTEs. Study will continue through the duration of norepinephrine infusion or until detection of MD. Treating Neuro ICU physicians will remain blinded to the lab and ECHO findings and will continue standard ICU management. This minimal risk study causes no undue harm to the patients.

Real-world cost-effectiveness of PCSK9 inhibitors

PI: M. Wesley Milks, MD
Mentor: Sheldon Retchin, MD, MSPH

The field of preventive cardiovascular medicine has recently experienced tremendous innovation¬ by the introduction of 2 novel, injectable monoclonal antibody agents of the proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) class that reduce atherogenic low density lipoprotein cholesterol (LDL-C) by an additional 60% beyond standard lipid-lowering therapies [1]. Outcomes data now demonstrate that the resultant LDL-C reduction with PCSK9i treatment is accompanied by a significant decrease in adverse cardiovascular outcomes [1]. As with many monoclonal antibody drugs, one predominant limitation is the high cost of treatment. Currently, the annual cost of PCSK9i therapy in 2017 exceeded $14,000, which has raised criticism of the cost-effectiveness of these therapies, with estimates of the cost-effective price in the range of $4,215[2]. Existing cost-effectiveness studies generally use simulated costs and anticipated benefits such as Markov modeling [2, 3], and as a result of model input variability, estimates have been highly discordant. Given how recently these agents were introduced (e.g. evolocumab was released commercially in 2015), real-world cost and outcomes data have until recently been unavailable. The goal of this study is to estimate the actual economic impact of PCSK9 inhibitors using the Truven Health MarketScan® Commerical Claims and Encounters Database. The potential benefit of this study would be to ascertain the actual rather than estimated costs of lipid lowering therapies including PCSK9i in comparison to the other costs of health care utilization, such as for downstream hospitalization, testing, and treatment related to complications of undertreated hyperlipidemia, such as incident or recurrent coronary disease and ischemic stroke.

Aspirin-triggered 15-epi-lipoxins in high risk pregnant women treated with low dose aspirin for preeclampsia prevention

PI: Kara Rood, MD
Mentor: Mark Landon, MD

Aspirin (ASA) is a cyclooxygenase inhibitor with antiplatelet and anti-inflammatory properties. Low-dose aspirin (LDA) has been recommended in high risk pregnancies to prevent preeclampsia (PE), but the precise mechanism of action and optimal dose is not known. One proposed theory for development of PE, suggests that signs and symptoms are due to an underlying inflammatory process. One of the more recent proposed mechanisms of action for use of ASA is its ability to initiate biosynthesis of novel anti-inflammatory mediators by means of interactions between endothelial cells and leukocytes. These mediators are classified as aspirin-triggered 15-epi-lipoxins (ATLs). Such compounds may account at least in part for some aspirin's clinical benefits, which are distinct from the well appreciated action of aspirin as a platelet inhibitor. We propose using stored maternal serum samples collected at The Ohio State Wexner Medical Center as part of the Maternal Fetal Medicine Unit Network RCT on High Risk Low Dose ASA trial to examine the levels of aspirin-triggered 15-epi-lipoxins (ATLs) in women who received low dose ASA for PE prevention. ATLs will be measured in OBGYN laboratory by ELISAs. There are no risks for participants and if results show that higher levels of ALTs are needed for PE prevention, then tailoring dose to achieve higher levels of ATLs in individual patients could benefit millions of pregnant women and their fetuses worldwide at a very low cost and risk.

Seizure prediction model in critically ill adult patients

PI: Jaysingh Singh, MD
Mentor: William Bell, MD

Purpose: Around 8-20% of critically ill adult patients experience electrographic seizures and their identification requires continuous electroencephalography (CEEG). However, the labor involved in maintaining and reading the CEEG recording is significantly higher than routine (or 30 minutes) duration EEG. Our current practice is to identify these electrographic seizures retrospectively with a delay of a few minutes to hours. Seizure prediction models could allow early detection of electrographic seizures and use CEEG resources more efficiently. Our aim is to develop and validate a seizure prediction model for use among critically ill adult patients. Study design: 10 CEEG records which captured electrographic seizures will be identified from EEG database and will be used for developing a prediction model. Steps involved in developing prediction model include preprocessing, feature extraction, EEG classifier using linear analysis and post-processing. Bipolar montage will be used for preprocessing. EEG findings like periodic or rhythmic discharges, interictal discharges will be extracted and used for the prediction model. Cost-sensitive support vector machine (SVM) will be used for classification of a preictal and interictal period. Developed model will be validated on a different set of EEG recordings for accuracy and false positive alarms. Risk: There is no documented patient harm since the model is developed using existing EEG data for which patient identifiers are not collected. Benefit: Currently, there are many seizure detection protocols, but prediction model provides the additional advantage with early identification and timely intervention with antiseizure therapy which could improve morbidity and mortality of patients.

Racial and Socioeconomic Disparities in Analgesic Use amongst Patients Presenting to the Emergency Department for Acute Renal Stone Disease

PI: Michael Sourial, MD
Mentor: Bodo Knudsen, MD

In the midst of a national opioid epidemic, a greater understanding of demographic and regional factors associated with opioid, narcotic, and painkiller prescription use is needed. Physicians are often faced with the dilemma of balancing the appropriate diagnosis, treatment, and pain management of a patient verses determination of drug-seeking behavior. As a first step, we propose a retrospective analysis of opioid prescription usage among adult patients presenting to the Ohio State University Hospital Emergency Department and University Hospital East Emergency Department between Jan 2013—Aug 2018 with a primary diagnosis of urolithiasis. The goal of this proposal is to summarize the percentage of ED encounters with analgesic/painkiller (narcotics & ketolorac) use during ED visit and at time of discharge, both overall by year and by patient characteristics (e.g. age, gender, race/ethnicity, insurance status, and ED). The main risks are data security/confidentiality which will be minimized with the use of password protected computers and limited user access. Results from this study will offer innovations in the form of 1) better understanding of the patient population presenting to the OSUWMC emergency department for urolithiasis; 2) longitudinal trends in opioid prescriptions for patients presenting to ED for kidney stones; 3) identification of racial/socioeconomic disparities associated with opioid use. Our department has never assessed urology-related narcotic use at EDs. Findings will provide a foundation for future research to better understand narcotic disparities in this patient population, potentially leading to interventions focused on increased sensitization in healthcare, cultural diversity training programs, and improved pain management.

Self-Efficacy in Hip Arthroscopy: A Randomized Trial of a Self-Efficacy Training Program

PI: W. Kelton Vasileff, MD
Mentor: Daniel Eiferman, MD

Our group will implement a randomized controlled trial to determine the usefulness of a self-efficacy training program for improving outcomes after arthroscopic hip surgery. Over a 4-month recruitment period, 128 patients who consent for hip arthroscopy will be recruited, then randomized into one of two groups (control vs experimental). Both groups will complete pre-operative patient-reported outcome measures to assess their (1) individual level of self-efficacy and (2) self-reported hip function. The control group will proceed with standard of care surgery, whereas the experimental group will complete a self-efficacy training program prior to their standard of care surgery. All participants will continue with any standard of care post-operative rehabilitation and medical follow-ups as recommended by their physician. Outcome measures will be recorded to a minimum of 6 months after surgery. Risks to the participants are minimal as all are undergoing elective standard arthroscopic hip surgery; the addition of a self-efficacy training program presents minimal additional risk. All participants are expected to report improved hip function after surgery, as previously demonstrated by this group. Additional benefits may include further improvement in hip function and self-efficacy from the training program. From this study we will hope to determine whether or not the self-efficacy training program is effective at improving post-surgical outcomes for hip arthroscopy, whether these improvements in outcomes led to a change in the patient-acceptable symptomatic state, and also whether the self-efficacy training program was effective at improving self-efficacy scores