Primary Presenter: Akaysha Joiner

Project Title: DAWN Clinic Surgical/Procedural Needs Assessment

Primary Mentor: Cristos Ifantides

Secondary Mentor(s):

Thematic Area: Global Health

Abstract:

The Dedicated to Aurora's Wellness and Needs (DAWN) Clinic serves the immigrant, uninsured, and underserved population of Aurora. The majority of their services focus on providing primary care screenings, a variety of specialty appointments, and connecting patients with resources to meet various needs (including health insurance, housing, and food stamps). Currently, the DAWN clinic is unable to provide procedures or surgeries at reduced costs for this patient population who is extremely vulnerable, especially if they are unable to obtain health insurance. This is a retrospective needs assessment study to determine the number of DAWN clinic patients needing surgical/procedural treatment. Initially, we focused on ophthalmology needs. This data was used to put together a proposal to ophthalmology providers to set up methods and resources for providing these treatments. Eventually, we hope to use the established ophthalmology relationship and protocol as a template to expand to other specialties at this clinic.

The ultimate goal is to create a working surgical/procedural unit that will be a reliable resource for the DAWN clinic. Data was collected via chart review in the electronic medical record system, Practice Fusion, then later, EPIC. We were looking at the assessment and plan of charts for patients seen on specialty nights (by Ophthalmology team specifically) from April 2016-April 2018 for two years of data collection. Data points include diagnoses (eye-related and risk factors/comorbidities, such as diabetes), treatment needed, treatment received, and demographic information. During this time period, we identified roughly 120 patients seen for ophthalmological services, about 20% of which needed procedures. Our goal was to identify the number of patients with surgical/procedural needs, the specific surgeries/procedures needed, and the frequency of these needs. By determining that a need did in fact exist, we were able to build a protocol for working with community providers to meet the need for cataract surgery and laser photocoagulation for diabetic retinopathy. There are no conflicts of interest to report, and COMIRB was not needed due to the nature of this project.

Primary Presenter: Kylie Van Hoesen

Project Title: An analysis of the factors associated with the greatest disease burden in the pediatric population seen at Khayelitsha Emergency Department between 2014-15.

Primary Mentor: Madiha Abdel-Maksound

Secondary Mentor(s): David Richards

Thematic Area: Global Health

Abstract:

Khayelitsha District Hospital (KDH) is a district level tertiary hospital that opened in February 2012. The hospital serves the partially informal township of Khayelitsha which means our new home in the Xhosa language. The 47-bed Emergency Department (ED) in the hospital serves more than 120 patients daily, with the pediatric patient population making up a significant percentage of the total number of patients seen in the ED. This study was conducted retrospectively to determine whether there is an association that exists between pediatric patients diagnosed with acute gastroenteritis (AGE), pneumonia and neonatal sepsis, and the following variables: sex, nature of referral, prematurity, and duration of time spent in the ED. A database which was collected over a span of six months from 1 November 2014 through 30 April 2015 and contained data for 325 pediatric patients seen in the Resuscitation Zone of KDH was analyzed to determine the associations noted above. The understanding of these associations will help to streamline protocols, make efficient use of limited resources, and implement system level changes at KDH to provide a higher standard of care for pediatric patients seen in the ED. The goal of this study is to shed light on opportunities available to minimize the morbidity and mortality of a vulnerable population.

Primary Presenter: Maggie Stalker

Project Title: Preeclampsia Alters Insulin Signaling Pathway Protein Expression in the High-Altitude Placenta

Primary Mentor: Colleen Julian

Secondary Mentor(s):

Thematic Area: Global Health

Abstract:

Background: Preeclampsia (PE) is associated with maternal morbidity and mortality globally, but especially in Bolivia where rates are third highest worldwide. The exact pathophysiology of PE is still unknown, but previous studies have shown insulin signaling pathway dysfunction and hypoxia as plausible mechanisms in PE development. This study aimed to examine protein expression of the insulin signaling pathway and correlate the proteins with hypoxia in PE placentas compared to normotensive controls at high-altitude to discover more about the PE pathogenesis.

Methods: Patients were recruited from the Hospital Materno-Infantil in La Paz, Bolivia (3,600-4,100m). Maternal blood samples were taken to measure erythropoietin receptor (EpoR) as a marker of hypoxia. Umbilical venous and arterial blood was sampled along with placental biopsies. Western capillary electrophoresis was used to measure protein expression of IRS1, pIRS1, IRS2, AKT, pAKT, and pGSK3B.

Results: 65 maternal-infant pairs with 29 PE cases and 36 controls were recruited for this study Compared to controls, PE placentas were found to have greater pAKT, greater pIRS1, and lower pGSK3B expression levels. There was also a trend seen in PE placentas having greater IRS2 expression levels, although not statistically significant. There was no significant difference in IRS1 or AKT protein expression between PE cases versus normotensive controls. There was a negative correlation between IRS1, pIRS1, IRS2 with EpoR. There was a positive correlation seen between pGSK3B with EpoR. There was no correlation between Akt and EpoR.

Conclusion: PE placentas showed dysfunction in the insulin signaling cascade concerning for insulin resistance. Hypoxia was determined to be a significant factor in this insulin signaling pathway, suggesting that hypoxia can interfere with normal functioning of this cascade. This study demonstrated how insulin signaling disruption and hypoxia can play a role in the pathophysiology of PE at high altitude.

Primary Presenter: Mehdi Bandali

Project Title: An analysis of the factors associated with the greatest disease burden in the pediatric population seen at Khayelitsha Emergency Department between 2014-15.

Primary Mentor: Leana May

Secondary Mentor(s): Madiha Abdel-Maksoud, David Richards

Thematic Area: Global Health

Abstract:

Khayelitsha District Hospital (KDH) is a district level tertiary hospital that opened in February 2012. The hospital serves the partially informal township of Khayelitsha which means our new home in the Xhosa language. The 47-bed Emergency Department (ED) in the hospital serves more than 120 patients daily, with the pediatric patient population making up a significant percentage of the total number of patients seen in the ED. This study was conducted retrospectively to determine whether there is an association that exists between pediatric patients diagnosed with acute gastroenteritis (AGE), pneumonia and neonatal sepsis, and the following variables: sex, nature of referral, prematurity, and duration of time spent in the ED. A database which was collected over a span of six months from 1 November 2014 through 30 April 2015 and contained data for 325 pediatric patients seen in the Resuscitation Zone of KDH was analyzed to determine the associations noted above. The understanding of these associations will help to streamline protocols, make efficient use of limited resources, and implement system level changes at KDH to provide a higher standard of care for pediatric patients seen in the ED. The goal of this study is to shed light on opportunities available to minimize the morbidity and mortality of a vulnerable population.

Primary Presenter: Natalie Lays

Project Title: An analysis of the factors associated with the greatest disease burden in the pediatric population seen at Khayelitsha Emergency Department between 2014-15

Primary Mentor: Madiha Abdel-Maksoud

Secondary Mentor(s):

Thematic Area: Global Health

Abstract:

Khayelitsha District Hospital (KDH) is a district level tertiary hospital that opened in February 2012. The hospital serves the partially informal township of Khayelitsha which means our new home in the Xhosa language. The 47-bed Emergency Department (ED) in the hospital serves more than 120 patients daily, with the pediatric patient population making up a significant percentage of the total number of patients seen in the ED. This study was conducted retrospectively to determine whether there is an association that exists between pediatric patients diagnosed with acute gastroenteritis (AGE), pneumonia and neonatal sepsis, and the following variables: sex, nature of referral, prematurity, and duration of time spent in the ED. A database which was collected over a span of six months from 1 November 2014 through 30 April 2015 and contained data for 325 pediatric patients seen in the Resuscitation Zone of KDH was analyzed to determine the associations noted above. The understanding of these associations will help to streamline protocols, make efficient use of limited resources, and implement system level changes at KDH to provide a higher standard of care for pediatric patients seen in the ED. The goal of this study is to shed light on opportunities available to minimize the morbidity and mortality of a vulnerable population.

Primary Presenter: Nguyen Lu

Project Title: Cardiac Surgery Publications in Africa Over the Last 20 years: A Literature Review

Primary Mentor: Yihan Lin

Secondary Mentor(s):

Thematic Area: Global Health

Abstract:

There is a significant burden of surgically correctable cardiovascular disease in Africa. The goal of this research was to review the last 20 years of literature on this topic. A systematic search was performed using PubMed, Embase and African Index Medicus for the period 1996€“2016. Publications came from 29 countries, all of different income brackets. Research output increased by 15-fold over the 20-year time period, with the majority of publications authored by local teams (71.4%) compared to visiting (4.9%) and mixed teams (23.7%). Although increasing, clinical reporting on cardiac surgery is still limited. Increased publication of results should be encouraged to better benchmark capacity and improve research capacity.

Primary Presenter: Scott Stuart

Project Title: "Intermittent Treatment of BRAFV600E Melanoma Cells Delays Resistance by Adaptive Resensitization to Drug Rechallenge"

Primary Mentor: Leanna May

Secondary Mentor(s): Natalie Ahn at University of Colorado, Boulder

Thematic Area: Basic Biomedical Science

Abstract:

Melanoma patients receiving drugs targeting BRAFV600E and MEK1/2 invariably develop resistance and continue progression. Based on preclinical studies, intermittent treatment involving alternating periods of drug withdrawal and rechallenge has been proposed as a method to delay the onset of resistance. The beneficial effect of intermittent treatment has been attributed to drug addiction, where drug withdrawal reduces the viability of resistant cells due to MAP kinase pathway hyperactivation. However, the mechanistic basis of the intermittent effect is incompletely understood. We show that intermittent treatment with the BRAFV600E inhibitor, LGX818/encorafenib, suppresses growth compared to continuous treatment in human melanoma cells engineered to express BRAFV600E, p61-BRAFV600E, or MEK2C125 oncogenes. Analysis of the BRAFV600E-overexpressing cells shows that, while drug addiction clearly occurs, it fails to account for the advantageous effect of intermittent treatment. Instead, growth suppression is best explained by resensitization during periods of drug removal, followed by cell death after drug readdition. Continuous treatment leads to transcriptional responses prominently associated with chemoresistance in melanoma. By contrast, cells treated intermittently reveal a subset of transcripts that reverse expression between successive cycles of drug removal and rechallenge, and include mediators of cell invasiveness and the epithelial to mesenchymal transition. These transcripts change during periods of drug removal by adaptive switching, rather than selection pressure. Resensitization occurs against a background of sustained expression of melanoma resistance genes, producing a transcriptome distinct from that of the initial drug-naiÌˆve cell state. We conclude that phenotypic plasticity leading to drug resensitization can underlie the beneficial effect of intermittent treatment.

Primary Presenter: Stephanie Cung

Project Title: In-vivo skeletal muscle mitochondrial function in Klinefelter syndrome

Primary Mentor: Shanlee Davis

Secondary Mentor(s):

Thematic Area: Clinical Science

Abstract:

Klinefelter syndrome (XXY) occurs in 1 in 600 males, resulting in testosterone deficiency and a high prevalence of insulin resistance. Testosterone deficiency in men is a known cause of insulin resistance, and mitochondrial dysfunction is hypothesized to mediate this relationship. The aim of this cross-sectional study was to evaluate muscle mitochondrial function in XXY compared with male controls. Twenty-seven boys with XXY (age 14.7€€1.8 years) were compared with 87 controls (age 16.9€€0.9). In-vivo calf muscle mitochondrial function was assessed via phosphorus magnetic resonance spectroscopy (31P-MRS) following 90 s of isometric 70% maximal exercise. Multiple linear regression was used to compare 31P-MRS outcomes (ADP and phosphocreatine (PCr) time constants, rate of oxidative phosphorylation (Oxphos), and Qmax or the maximal mitochondrial function relative to mitochondrial density) between groups after adjusting for age differences. There were no statistically significant differences in the mitochondrial outcomes of ADP, Oxphos, PCr, and Qmax between the groups. There were also no differences in a sensitivity analysis within the XXY group by testosterone treatment status. In this study, in-vivo postexercise skeletal muscle mitochondrial function does not appear to be impaired in adolescents with XXY compared with controls and is not significantly different by testosterone treatment status in XXY.

Primary Presenter: Taylor Davis

Project Title: REDCap for National Rheumatic Heart Disease Registry

Primary Mentor: Yihan Lin

Secondary Mentor(s): R. Morton Bolman, MD, Ceeya Bolman, RN

Thematic Area: Global Health

Abstract:

Background: Rheumatic heart disease (RHD) is the most common cause of acquired cardiovascular disease (CVD) among young populations in low-income countries. Team Heart began performing cardiac surgical interventions in Rwanda in 2007, necessitated by the large burden of severe disease. The growing population of post-operative patients and of patients screened for RHD require a method for collecting high-quality, epidemiologic data. Disease registries have been shown to improve health outcomes, enhance disease surveillance, increase healthcare utilization, and strengthen health systems globally. We sought to create a rheumatic heart disease registry for Rwanda.

Methods: The methodology of registry development followed stages outlined by Evatt (2005). 1) Establish goals of the registry and prepare action plan. 2) Selection system of data collection. 3) Determine data content and design data collection form. 4) System trainings. 5) Collect and analyze data. 6) Review the registry system.

Discussion: The objectives of the registry are to create a centralized system for comprehensive disease data, improve healthcare access and outcomes for RHD patients, and provide a source of aggregate data to better inform policy change and further research with the goal of eradication of endemic RHD in Rwanda. With the initial surgical registry now accessible, future directions include collaborating with the Rwanda Biomedical Center (RBC) on projects and research including investigating pregnancy outcomes of post-operative patients in the context of their anticoagulation regimens.

Primary Presenter: William Mundo

Project Title: Hypoxia-induced inhibition of mTORC1 activity in the developing lung: a possible mechanism for the developmental programming of pulmonary hypertension

Primary Mentor: Colleen Julian

Secondary Mentor(s):

Thematic Area: Clinical Science

Abstract:

Perinatal hypoxia induces permanent structural and functional changes in the lung and its pulmonary circulation that are associated with the development of pulmonary hypertension (PH) in later life. The mechanistic target of the rapamycin (mTOR) pathway is vital for fetal lung development and is implicated in hypoxia-associated PH, yet its involvement in the developmental programming of PH remains unclear. Pregnant C57/BL6 dams were placed in hyperbaric (760 mmHg) or hypobaric chambers during gestation (505 mmHg, day 15 through postnatal day 4) or from weaning through adulthood (420 mmHg, postnatal day 21 through 8 wk). Pulmonary hemodynamics and right ventricular systolic pressure (RVSP) were measured at 8 wk. mTOR pathway proteins were assessed in fetal (day 18.5) and adult lungs (8 wk). Perinatal hypoxia-induced PH during adulthood, even in the absence of a sustained secondary hypoxic exposure, as indicated by reduced pulmonary artery acceleration time (PAAT) and peak flow velocity through the pulmonary valve, as well as greater RVSP, right ventricular (RV) wall thickness, and RV/left ventricular (LV) weight. Such effects were independent of increased blood viscosity. In fetal lung homogenates, hypoxia reduced the expression of critical downstream mTOR targets, most prominently total and phosphorylated translation repressor protein (4EBP1), as well as a vascular endothelial growth factor, a central regulator of angiogenesis in the fetal lung. In contrast, adult offspring of hypoxic dams tended to have elevated p4EBP1 compared with controls. Our data suggest that inhibition of mTORC1 activity in the fetal lung as a result of gestational hypoxia may interrupt pulmonary vascular development and thereby contribute to the developmental programming of PH