



August 6, 2018  
Brody Commons

---

**21ST ANNUAL**  
MEDICAL STUDENT  
RESEARCH DAY

# *Acknowledgments*

---

The Brody School of Medicine Summer Scholars Program would like to express its sincere gratitude to the following individuals and participating faculty of the following departments for their support of the 2018 Program. Those listed provided financial support for student stipends, research resources, administrative support and/or funds for the 2018 Medical Student Research Day. These generous contributions make it possible for BSOM students to learn and make their own contributions to the field of medicine through scholarly pursuits.

Dr. Davis Allen, Rosemary Davis Fund

Dr. Nitin Gupta, Gupta Fund

Mrs. Mousami Gupta, Gupta Fund

BSOM Department of Academic Affairs

Department Biochemistry and Molecular Biology

Department of Communication Sciences and Disorders, CAHS

Department of Emergency Medicine

Department of Internal Medicine

Department of Pediatrics

Department of Physical Medicine and Rehabilitation

Department of Physiology

Department of Radiation Oncology

Department of Surgery

Ms. Jenna Garris, Office of Medical Education

Mr. Gary Vanderpool, Executive Vice Chancellor, Health Sciences

Administration & Finance

# FACTORS ASSOCIATED WITH THE PREVALENCE AND PROGRESSION OF IMPAIRED GLUCOSE TOLERANCE AND TYPE 2 DIABETES IN PATIENTS REFERRED TO THE VANDERBILT PEDIATRIC PREDIABETES CLINIC

S. NASEERUDDIN AHMED, CHELSEA N. LAWSON, AND ASHLEY H. SHOEMAKER

## BACKGROUND

Diagnostic criteria for Type 2 Diabetes (T2D) in pediatric patients is not well established and lab markers have been shown to poorly correlate with each other. In addition, long term progression of impaired glucose tolerance (IGT) and T2D in children has not been fully explored.

## OBJECTIVE

It was hypothesized that factors such as change in BMI may be associated with the long-term progression of glucose tolerance into worsened or resolved states.

## METHODS

A retrospective chart review of 260 patients referred to the Vanderbilt Pediatric Prediabetes Clinic for HbA1C levels of  $\geq 5.7\%$  was conducted.<sup>1</sup> Patients were divided into groups of Normal Glucose Tolerance (NGT), IGT, or T2D based on American Diabetes Association criteria, and non-parametric tests were used to analyze demographic data and clinical visit findings from initial visits and follow ups.<sup>1</sup>

## RESULTS

Of the patients seen, 27.3% had IGT and 6.5% had T2D. Patients with IGT and T2D were older than those with NGT (NGT:  $11.9 \pm 2.9$  vs. IGT:  $13.1 \pm 2.2$  vs. T2D:  $13.2 \pm 3.0$ ,  $p=0.004$ ) and were more likely to be female (NGT: 51.2% vs. IGT: 59.2% vs. T2D: 82.4%,  $p=0.036$ ). Patients with IGT and T2D also had higher BMIs (NGT:  $32.7 \pm 8.4$  vs. IGT:  $36.3 \pm 7.2$  vs. T2D:  $39.8 \pm 10.6$ ,  $p=0.001$ ) and were more likely to have a 1st degree relative with T2D (NGT: 30.2% vs. IGT: 49.3%, TD2: 47.1%,  $p=0.014$ ). Patients with IGT and T2D had higher HbA1C levels, fasting glucose, and 2 hour glucose levels ( $p<0.001$ ) but these three measures were poorly correlated with each other. The 5 patients that progressed to T2D over time had an average increase in BMI of  $1.51 \pm 2.4$  and increase in HbA1C of  $1.46\% \pm 1.8$  over an average of  $14.2 \pm 7.3$  months, while the 4 patients that regained NGT had an average decrease in BMI of  $0.48 \pm 2.5$  and a change in HbA1C of  $0 \pm 0.29$  over an average of  $6 \pm 5.1$  months. There were 15 patients with continuing IGT and 2 that progressed to T2D that were lost to follow-up.

## CONCLUSION

These data suggest that age, sex, BMI, and family history may contribute to susceptibility to IGT and T2D in children, and that increased BMI and HbA1C over time correlates with progression to T2D.



# DEVELOPMENT OF CRISPR-CAS CONSTRUCTS TO INTERROGATE RACE-RELATED DIFFERENTIAL SPLICING OF ABLIM3 IN PROSTATE CANCER

JENNIFER AWUKU, MUTHANA AL ABO , JENNIFER A. FREEDMAN AND STEVEN R. PATIERNO

## BACKGROUND

Prostate cancer affects one in nine men during their lifetime and kills approximately 29,430 men each year in the United States. African American (AA) men are more likely to experience a more aggressive form of prostate cancer and are also more likely to die from the disease compared to Caucasian American (CA) men. These differences persist after controlling for differences in social, lifestyle, and structural determinants of health.

## OBJECTIVE

This work addresses the urgent need to interrogate molecular mechanisms contributing to racial disparity in prostate cancer.

## METHODS

We have recently shown that race-related alternative splicing (AS) in prostate cancer cells can contribute to this racial disparity in prostate cancer. Exon array analysis of prostate cancer specimens has identified AS differences between prostate cancer in AA and CA patients. One of these AS events involves exon 15 of Actin Binding LIM Protein Family Member 3 (ABLIM3). ABLIM3 may play a contributing role in cancer growth and aggressiveness. To study the importance of ABLIM3 AS to prostate cancer cell biology, we are using CRISPR-Cas9 technology to engineer prostate cancer cells that express the ABLIM3 isoform lacking exon 15. In this method, Cas9 will introduce double-strand breaks in the genome at exon 15 of ABLIM3 and homology directed repair will delete exon 15.

## RESULTS

To date, we have designed and cloned the guide RNA plasmid and the donor homologous recombinant plasmid that will be inserted into the prostate cancer cell lines to be edited. In addition, the guide RNA was inserted into the plasmid. Furthermore, the homologous recombination (HR) donor sequence was cloned alongside the selection marker, Puromycin. Transfection of the CRISPR-Cas and HR donor plasmids into PC3 prostate cancer cells and analysis of resulting alterations in the growth, aggressiveness, and drug response of these cells is currently underway. We successfully developed the CRISPR-Cas constructs needed to express the ABLIM3 isoform lacking exon 15.

## CONCLUSION

This discovery could aid in development of new biomarkers or therapeutic agents based on AS of ABLIM3 that could ultimately improve outcomes for men with prostate cancer driven by this mechanism.

# **DIRECT PERITONEAL RESUSCITATION IN TRAUMA PATIENTS RESULTS IN SIMILAR RATE OF INTRA-ABDOMINAL COMPLICATIONS COMPARED TO CONVENTIONAL RESUSCITATION METHODS**

**JACOB EDWARDS, MD; MARISSA BURCHETTE, BS; AND NATHANIEL POULIN, MD**

## **BACKGROUND**

Traumatically injured patients who undergo damage control surgery have a propensity for complicated abdominal closures and high risk of intra-abdominal complications. Studies have shown that management of these open abdomens with direct peritoneal resuscitation (DPR) reduces intra-abdominal complications and accelerates abdominal closure. However, no study has specifically identified if there is a difference in intra-abdominal infection rates.

## **OBJECTIVE**

The management of open abdomens in trauma patients undergoing damage control surgery with direct peritoneal resuscitation would decrease the rate of intra-abdominal abscesses, fistulas, dehiscence, evisceration, and hernias.

## **METHODS**

A retrospective chart review was performed on patients in the Vidant Medical Center Trauma Registry. Selected patients underwent damage control surgery from January 2013 to February 2018. Fifty patients were identified who underwent damage control surgery with direct peritoneal resuscitation, and matched to seventy controls by gender, race, age, BMI, past medical history, mechanism of trauma, and injury severity score.

## **RESULTS**

Complete data analysis is still pending but based upon preliminary results the formation of hernias in trauma patients who underwent direct peritoneal resuscitation following damage control surgery was higher than controls whose open abdomens were managed with conventional resuscitation methods (DPR: 30% vs. 10%;  $p=.0095$ ). No difference was found between groups in the rate of formation of intra-abdominal abscesses (DPR: 24% vs. 29%;  $p=.7271$ ) or fistulas (DPR: 10% vs. 10%;  $p=1.000$ ). Furthermore, there was no difference in the rate of dehiscence (DPR: 6% vs. 13%;  $p=.3545$ ) or evisceration (DPR: 2% vs. 1%;  $p=.8095$ ) between groups.

## **CONCLUSION**

The use of direct peritoneal resuscitation in the management of open abdomens on the population studied did not result in different patient outcomes. Therefore, traditional resuscitative measures for damage control surgery may not be inferior to damage control surgery with DPR.

# PREDEFINED ANGLES AND A REVISED APPLES MNEMONIC IMPROVE PERFORMANCE TIME FOR THE OUT OF PLANE APPROACH ON ULTRASOUND GUIDED PERIPHERAL NERVE INTERVENTIONS

**WILLIAM BRADER MS2; MICHAEL MCIVER MD; KIMBERLY RATHBUN MD, MPH, PHD; VIVEK SINDHI MD, MBA; NATALIE KARR MS3; JOHN NORBURY MD**

## BACKGROUND

Ultrasound guided needle placement is a widely used technical skill but it is difficult to learn. There is currently no widely accepted, standardized approach to teaching ultrasound guided needle nerve blocks.

## OBJECTIVE

To determine if giving novices predefined angles would improve performance time and accuracy when learning and performing ultrasound guided procedures. A secondary objective was to determine whether participants thought the APPLES (approach, position, perpendicular, lift, entry, sweep) mnemonic was a helpful guide for performing the procedure.

## METHODS

Participants were randomized into 4 groups and given instructions for the first trial based on method and depth of target. For the second attempt, each participant was given an approach angle and a distance from the probe to insert the needle. For both trials, the participant had 15 seconds to hit the target. Videos of each attempt were reviewed by 2 blinded physicians to determine accuracy and time to target. After both trials, the participants were explained the APPLES mnemonic and asked to complete a survey indicating if they thought the mnemonic would be helpful when learning both methods for ultrasound guided procedures. A Mann Whitney U test was used to compare performance times and a Fisher's Exact test was used to compare accuracy.

## RESULTS

Of the participants who received the predetermined angle and distance for the out of plane approaches, those performance times were statistically significantly lower than the performance times of the participants who did not receive angles and distance for the out of plane approach.

Of the 30 participants who received the predetermined angle for the 3cm out of plane approach, 18 participants hit the target while of the 30 participants who did not receive the angles for this approach, only 9 participants hit the target. There was a statistically significant association between receiving the predetermined angle and hitting the target for this approach.

95% of participants found the APPLES mnemonic helpful for learning and performing ultrasound guided procedures.

96.67% of participants indicated that being given the predetermined angles/distances would be helpful in learning and performing ultrasound guided procedures.

# AN IMPROVED PHANTOM NERVE MODEL FOR SIMULATED ULTRASOUND GUIDED INTERVENTIONS

**WILLIAM BRADER MS2; JOHN NORBURY MD; MICHAEL MCIVER MD; VIVEK SINDHI MD, MBA; KIMBERLY RATHBUN MD, MPH, PHD**

## BACKGROUND

Ultrasound guided procedures are very difficult for beginners to master in terms of accuracy and efficiency. Phantom models allow for novices to practice ultrasound guided procedures before attempting to complete one on a live patient. Mass produced phantom models are incredibly expensive. There is not a realistic phantom model that is easy to construct in terms of simulating the appearance of a nerve.

## OBJECTIVE

Ultrasound guided nerve blocks are a common procedure done for both diagnostic and therapeutic purposes. Ultrasound phantoms are frequently used in procedural teaching to improve learner's familiarity and comfort with the procedure before performing the procedure on patients. A few nerve block phantoms have been developed. We believe we have an improved model based on ease of construction combined with a more realistic nerve appearance.

## METHODS

The nerve block model was made with a core of hot dog embedded in a gelatin mold. Metamucil powder was added to improve consistency. Food dye was added to improve opacity. A trial and error of many other objects was conducted before settling on the hot dog core. Objects tried included fishing line, electric cable, rope, twine, and various candy.

## RESULTS

This nerve block model realistically simulates the sonographic appearance of a nerve and avoids the risk of bacterial contamination that exists with poultry or pork meat. The hot dog core allowed for most realistic simulation of nerve block procedures as it provided the least amount of posterior acoustic resonance. This allows the beginner to access the inferior side of the nerve for good practice of blockage or hydrodissection.

## CONCLUSION

This nerve block phantom is inexpensive and easily constructed. It allows medical students and residents to realistically simulate nerve-targeting procedures to increase their comfort level and skill before attempting procedures on patients.

# PLASMA NITRIC OXIDE LEVELS IN DIABETIC RETINOPATHY

**KAITLYN BROBST, BS; CASSANDRA WARDEN, BS; SABRINA MITCHELL, PHD; MILAM BRANTLEY, MD, PHD; DEPARTMENT OF OPHTHALMOLOGY AND VISUAL SCIENCES, VANDERBILT UNIVERSITY MEDICAL CENTER**

## BACKGROUND

Evidence suggests arginine metabolism is altered in patients with type 2 diabetes with diabetic retinopathy (DR). However, the mechanisms by which this dysregulation occurs are incompletely defined. Through untargeted metabolomics, our lab previously observed significant increases in plasma arginine and citrulline in DR patients compared to diabetic controls. Arginine is a substrate for nitric oxide synthase in a reaction producing nitric oxide (NO) and citrulline. Nitric oxide is a potent vasodilator and causal factor of vascular damage when released in excess.

## OBJECTIVE

We hypothesized that altered nitric oxide synthase activity could contribute to the elevated plasma arginine and citrulline metabolites in DR patients.

## METHODS

To test this hypothesis, we recruited patients with type 2 diabetes with or without DR, and non-diabetic controls. DR patients were classified as non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR). A nitrate reduction assay was performed using patient plasma to indirectly measure the activity of nitric oxide synthase via NO metabolite concentrations. Plasma NO levels were compared among the study groups.

## RESULTS

In logistic regressions adjusting for age, sex, diabetes duration, and HbA1c, plasma NO levels were significantly lower in patients with type 2 diabetes compared to non-diabetic controls ( $p=0.477$ ). There were no differences in plasma NO levels between DR patients and diabetic controls ( $p=0.891$ ) or between NPDR and PDR patients ( $p=0.126$ ).

## CONCLUSION

These results suggest that the higher plasma levels of arginine and citrulline previously observed in DR patients are not associated with altered nitric oxide synthase activity.



# PELVIC RADIATION THERAPY CAUSES BOTH DECREASED BLADDER AND INCREASED URETHRAL CONTRACTION IN FEMALE RATS

LINDSEY BURLESON, SHELBY POWERS, MICHAEL ODOM, JOHANNA HANNAN, PHD

## BACKGROUND

Women with cervical and endometrial cancers treated with radiation therapy can experience injury and fibrosis from surrounding tissues leading to genitourinary dysfunction. Fibrosis has been implicated in chronic vaginal and bladder diseases, but little research has been performed to illustrate both the short and long-term effects of pelvic radiation induced injury in females.

## OBJECTIVE

We determined if genitourinary tissues, such as vaginal, bladder and urethra, experienced a decrease in smooth muscle contraction and vaginal blood flow 4 weeks after pelvic radiation. We predict that radiation will cause an early decrease in vaginal, bladder, and urethral tissue contraction and vaginal blood flow to reflect the acute phase of fibrosis formation.

## METHODS

Female Sprague-Dawley rats (10 weeks) received one 20 Gy dose of x-ray irradiation (control n=5, radiated n=8). At 4-weeks post-irradiation, electric field stimulated increases in vaginal blood flow were measured using a laser doppler probe placed against the anterior wall of the vagina and normalized to mean arterial pressure. Tissue bath experiments assessed vaginal, bladder, and urethral smooth and striated muscle vasoreactivity. In vaginal tissue, we tested adrenergic and cholinergic contraction responses and nitric oxide-mediated relaxation responses. Bladders were subjected to cholinergic contraction in the presence and absence of an anti-muscarinic inhibitor. Urethral smooth and skeletal muscle was assessed using cholinergic agonists and ryanodine receptor-mediated contraction. Contractile properties of all tissues were evaluated by electric field stimulation.

## RESULTS

Vaginal blood flow was unchanged between the pelvic radiation group and the control group. Similarly, pelvic radiation did not alter vaginal smooth muscle contraction or relaxation. Bladder smooth muscle showed decreased cholinergic-mediated contraction as well as a decrease in electric field stimulated contraction at frequencies greater than 4 Hz ( $p < 0.05$ ). The smooth muscle of the urethras experienced an increase in cholinergic-mediated contraction and electric field stimulation greater than 8 Hz. Caffeine-induced contractions increased in magnitude in urethral sphincters ( $p < 0.001$ ).

## CONCLUSION

At 4 weeks post-pelvic radiation therapy, vaginal parameters remain unaffected while bladder smooth muscle experiences a decrease in contraction and urethral muscle increases in contraction. These findings indicate that bladder injury may precede female sexual dysfunction after pelvic radiation.

# NEUROLEPTANALGESIA WITH BUTYROPHENONE ANTIPSYCHOTICS FOR ACUTE ABDOMINAL PAIN: A SYSTEMATIC REVIEW AND PLANNED META-ANALYSIS

ALBERTO A. CASTRO BIGALLI, MSC, ABBAS M. KHAN, MD, KERRY SEWELL, MSLS, ANDREW C. MILLER, MD

## BACKGROUND

Administration of opioids (with later prescription) in the ED has been linked to an increased risk of opioid abuse. Cultivating effective analgesia techniques that limit narcotic consumption is needed.

## OBJECTIVE

Neuroleptanalgesia involves combining an opiate (eg. fentanyl) with a butyrophenone neuroleptic drug (eg. haloperidol, droperidol, olanzapine). This project seeks to determine if neuroleptanalgesia provides effective analgesia while decreasing opiate consumption in acute abdominal pain patients.

## METHODS

For this systematic review with planned meta-analysis, eligible studies were prospective randomized trials of adult patients ( $\geq 18$  years) with acute abdominal pain in the ED, ICU, or immediate post-operative setting. Butyrophenone administration was intravenous or intramuscular. Primary endpoints were pain control and opiate consumption. Secondary outcomes were patient satisfaction with analgesia, admission rates, ED length-of-stay (LOS), hospital LOS, and side-effects (extrapyramidal, akathisia, cardiac). KS developed the structured search strategy for PubMed, Scopus, and Web of Science. ACM designed searches of LILACS, DOAJ, SID, TÜBİTAK ULAKBİM, and bibliographies. Searches were not limited by date, language, or publication status. Trial registries were searched to limit publication bias, including: ClinicalTrials.gov, WHO ICTRP, and ANZCTR. Grey literature was only included in quantitative analysis if authors provided primary data. Risk of bias was assessed using RoB 2.0: "Revised tool for Risk of Bias in randomized trials".

## RESULTS

Database searching identified 7217 records, and 55 additional records were identified through other searches. 981 duplicates were removed, 6291 records were screened, and 6284 records were excluded. Seven studies were assessed for quantitative synthesis (meta-analysis). The presence of significant methodological differences between studies precluded performance of the planned meta-analysis, thus the systematic review was completed. In ED patients, neuroleptanalgesia improved analgesia and decreased overall opiate consumption, while decreasing ED LOS and admission requirements. Results were particularly pronounced for patients with gastroparesis, cyclical vomiting syndrome, and cannabinoid hyperemesis. For post-operative patients, adding a butyrophenone to the PCA regimen improved patient analgesia and satisfaction, and decreased opiate consumption without increasing adverse effects.

## CONCLUSION

Neuroleptanalgesia effectively improved analgesia and decreased opiate consumption in patients with acute abdominal pain. ED Data suggests the greatest benefit for patients with gastroparesis, cyclical vomiting syndrome, and cannabinoid hyperemesis.

# MORPHOLOGY OF THE MUSCULUS UVULAE IN VIVO USING MRI AND 3D MODELING AND PRELIMINARY COMPARISON TO CLEFT PALATE ANATOMY

JOSHUA Y. CHEN, BS, JAMIE L. PERRY, PHD, KATELYN KOTLAREK, MS, ABIGAIL HAENSSLER, MS, XIANGMING FANG, PHD, DAVID P. KUEHN, PHD, BRADLEY P. SUTTON, PHD

---

## OBJECTIVE

To investigate the musculus uvulae in adults with normal velopharyngeal anatomy in vivo and to examine sex and race effects on the muscle morphology. We also present a preliminary comparison of the musculus uvulae in adults with normal velopharyngeal anatomy to adults with a history of repaired cleft palate.

## METHODS

3D MRI data and Amira 5.5 Visualization Modeling software were used to evaluate the musculus uvulae muscle in 70 participants without cleft palate and 6 participants with cleft palate. Muscle length, thickness, width, and volume were used for comparison among participant groups.

## RESULTS

ANCOVA analysis did not yield statistically significant differences in musculus uvulae length, thickness, width, or volume by race or sex among participants without cleft palate when the effect of body size was accounted for. Paired T-test revealed that the musculus uvulae in participants with cleft palate is significantly shorter ( $p = 0.008$ ) and has less volume ( $p = 0.002$ ) than participants without cleft palate.

## CONCLUSION

Our findings agree with previous findings of qualitative musculus uvulae morphology. We did not find any evidence that race or sex significantly influence the musculus uvulae. Differences in musculus uvulae in the cleft palate population may contribute to velopharyngeal insufficiency, leading to difficulty with speech production.

# A WEARABLE TELEMEDICINE DEVICE FEASIBLE FOR ACUTE STROKE ASSESSMENT: THE NEUROLOGY RESIDENT EVALUATION USING GOOGLE GLASS (NEUROEGG) STUDY

**WILLIAM CLARK, BA; JOSEPH CARRERA, MD; CONNOR WANG, BA; HAYDON PITCHFORD, BA; NICHOLE CHIOTA-MCCOLLUM, MD; BRADFORD B. WORRALL, MD, MSC AND ANDREW M. SOUTHERLAND, MD, MSC**

## **BACKGROUND**

Acute stroke patients require time-sensitive evaluations, which are often performed by providers lacking expertise in skilled neurological assessment. While conventional telemedicine is an established medium for remote supervision, Google Glass (GG) has emerged as a hands-free, wearable alternative. As part of the Neurology Resident Evaluation Using Google Glass (NeuroEGG) Study, we examined GG applicability in the inpatient acute stroke setting.

## **OBJECTIVE**

We hypothesize that GG is a feasible alternative to face-to-face observation for the supervision of neurology residents and evaluation of patients in the acute stroke setting.

## **METHODS**

We paired GG with Pristine Eyesight, a HIPPA-compliant application for live video teleconferencing (VTC). During inpatient acute stroke evaluations, neurology residents were simultaneously observed by a blinded supervising physician in-person and a second supervising physician via live VTC. We determined agreement between in-person and remote VTC evaluations via the intra- and inter-rater reliability of the NIH Stroke Scale (NIHSS) (Cohen kappa > 0.75).

## **RESULTS**

We evaluated 17 acute stroke patients in the Emergency Department, Stroke Unit and Neurological Intensive Care Unit. Total NIHSS scores between in-person and remote supervising physicians demonstrated almost perfect agreement beyond chance (Cohen's kappa=0.84; CI 0.73-0.96). Weighted kappa statistics for individual components of the NIHSS showed strong agreement for best gaze and motor leg (k=0.8-1.0); substantial agreement for motor arm, best language and sensory (k=0.6-0.8); and fair agreement for facial palsy and dysarthria (k=0.2-0.4). Extinction could not be evaluated due to sample size.

## **CONCLUSION**

Google Glasses allowed remote supervising physicians to provide reliable, hands-free teleconsultation to neurology residents in the inpatient acute stroke setting. The ability to inherit the residents' visual perspective introduces a novel approach to assess examination skills and to ensure patient safety. Logistical and time constraints resulted in slower than anticipated enrollment. As part of the NeuroEGG study, additional planned analyses include feasibility in the outpatient setting as well as resident and patient satisfaction. Our results with a wearable telemedicine device in a small single-center study call for feasibility testing in other health systems and clinical environments.

# CLINICAL MARKERS OF RENAL FUNCTION IN SICKLE CELL DISEASE

**KATHRYN CLARY; DR. DARLA LILES, MD; RAMATU SAMURA, MPH**

## BACKGROUND

Sickle Cell Disease (SCD) is an inherited hematological disorder in which abnormal hemoglobin causes red blood cells to become rigid and “sickle” shaped. Sick cells aggregate, obscure blood flow, and prevent oxygen delivery to organs. These blockages cause recurring episodes of severe pain and widespread organ damage. There are different forms of SCD, classified based on the number and type of abnormal hemoglobin produced. These are referred to as genotypes. Renal complications are a common manifestation of SCD, particularly among aging patients and HbSS patients. A few traditional markers of kidney dysfunction include high serum creatinine, low glomerular filtration rate (GFR), and proteinuria (protein in the urine). However, despite the prevalence of kidney dysfunction within the SCD population, numerous studies have described two notable features that exist among SCD patients: low serum creatinine and hyperfiltration of the glomerulus (high GFR).

## OBJECTIVE

The aim of this study was to characterize the differences in the clinical markers of renal function between SCD genotypes.

## METHODS

A retrospective chart review analyzed 115 adult SCD patients, ages 20 to 65, who were followed at the Leo Jenkins Cancer Center between January 1, 2013 and December 31, 2016 (67 HbSS and 48 HbSC or Hbβ+). Statistically significant relationships were found to exist between the HbSS genotype and low serum creatinine ( $p=0.007$ ; OR=3.38), hyperfiltration of the glomerulus ( $p=0.001$ ; OR=5.75), and a history of proteinuria ( $p=0.0003$ ; OR=4.85).

## RESULTS

Initial results found a higher prevalence of proteinuria in the HbSS population. This finding aligns with the existing literature and may be an indicator that kidney damage is present at higher levels within the HbSS population. Additionally, findings from this study suggest that the traditional definitions of serum creatinine and GFR may underestimate renal impairment in HbSS SCD patients.

## CONCLUSION

The differences found in serum creatinine levels and GFRs between the two groups suggest that genotype must be considered when interpreting laboratory values that assess for renal function. Additional studies are needed to determine the roles that hyperfiltration and serum creatinine play in glomerular damage among SCD patients.



# **SURVIVAL DIFFERENCES IN PATIENTS PRESENTING TO EASTERN NC EDS WHO RECEIVED INITIAL CANCER DIAGNOSIS**

**HANNAH L. CONLEY, RAVEN V. DELGADO, JUSTIN MCCALLEN, ELEANOR E. R. HARRIS, M.D., ANDREW JU M.D., KIMBERLY M. RATHBUN M.D., MPH**

## **BACKGROUND**

The survival outcomes in cancer are better in patients who are diagnosed at an early stage, which can potentially be detected through screening and routine visits to a primary care physician. However, patients with difficulty accessing care may be diagnosed with cancer more often in the Emergency Department (ED), and potentially at a later stage when survival outcomes may be worse. Characterization of the patients who are diagnosed with ED and analysis of their outcomes may potentially guide public policy.

## **OBJECTIVE**

We hypothesized that patients who present to the ED and received their initial cancer diagnosis there will have a shorter survival time than their counterparts who received diagnoses outside the ED.

## **METHODS**

Data was obtained on retrospective review from ED visits in the Vidant system in eastern North Carolina made during 2014-2015 that were associated with an oncological-related ICD-9 code. Patient characteristics, cancer characteristics, and survival outcomes were collected. Factors significant on univariate analysis were included in a multivariate analysis of survival outcomes. Statistical analyses were performed using MedCalc.

## **RESULTS**

Initial diagnosis in the ED was recorded in 38.5% of patients analyzed (n=400/1039). Mean survival time following diagnosis was significantly lower in individuals diagnosed in the ED (26 months vs. 54 months,  $p < .0001$ ), men vs women (39 months vs. 50 months,  $p < .0001$ ), and patients with a Charlson Comorbidity Index of greater than 8 (30 months vs. 53 months,  $p < .0001$ ).

## **CONCLUSION**

Patients who received a cancer diagnosis in the ED at our institution have significantly shorter survival times from diagnosis. Further investigation into the public health factors that may contribute to patients receiving their cancer diagnosis in the ED should be conducted, with comparison to the outcomes seen in other regions of the country.

# PREVALENCE AND PREDICTORS OF MALNUTRITION AMONG CHILDREN IN THE PALAJUNOJ VALLEY, GUATEMALA

DYLAN FLOOD, EMILY KRAGEL, SABRINA LINGEMAN, NATALIE CONSTANTINE, KEVIN HILL

---

## BACKGROUND

Guatemala has child malnutrition and stunting rates that are among the highest in the world, particularly in rural, indigenous communities.

## OBJECTIVE

The objective of this study was to estimate the prevalence of malnutrition in the indigenous population, and the health, environmental and socio-demographic determinants of stunting in indigenous children below the age of five in the Palajunoj Valley, Guatemala.

## METHODS

Children under the age of 5 (n = 93) were examined to ascertain height-for-age, and a questionnaire was completed with each mother (n = 93). The questionnaire collected data on household nutritional adequacy, infectious disease risk and burden, prenatal care, and breastfeeding practices.

## RESULTS

Among 93 children, the prevalence of stunting was 56.2%. The proportion of households with inadequate nutritional intake was 70.5%, and 49.5% reported high incidence of child illness. Multivariate analysis for association with stunting yielded a significant model (P=0.024), which correctly predicted 65.6 percent of the cases of stunting. Nutritional adequacy, prenatal care and breastfeeding practices were the variables that had the greatest impact on stunting. Inadequate prenatal care was found to significantly contribute to the increased self-report of illness, with a P-value of 0.021 and OR of 3.180. Stunting was also associated with increased incidence of illness self-report.

## CONCLUSION

In conclusion, children under 5 in the Palajunoj valley consume inadequate quantities and varieties of foods to prevent stunting and the associated increase in susceptibility to infection. It is necessary to increase local healthcare resources, and to develop programs to provide adequate nutrition via sponsorship of school meals and distribution of supplements and vitamins to families.

# CHRONIC EXPOSURE TO ORGANOPHOSPHATE PESTICIDES AND THEIR ASSOCIATION WITH OBESITY, TYPE 2 DIABETES MELLITUS, AND METABOLIC SYNDROME

**BRANDON L. FOX, LISA M. DOMICO PHD, KIMBERLY A. KEW PHD, ANNE M. SPUCHES PHD, CAITLIN D. PALMER, MOHAMMAD K. SARSOUR, SHEA R. GOLDEN, WALTER J. PORIES MD**

## BACKGROUND

During the past 2 decades, there has been a continuous increase in the prevalence of obesity, Type 2 diabetes Mellitus (T2DM), and metabolic syndrome (MetS) across the United States. The prevailing explanation behind these chronic metabolic disease epidemics was attributed to modifiable (diet, exercise) and non-modifiable (genetics, aging) risk factors. However, these risk factors alone do not completely account for the current epidemic of metabolic diseases. In search for an explanation beyond lifestyle and genetic risk factors an increasing amount of research has focused on possible environmental factors that may play a role in the multiple metabolic disease epidemics. One environmental factor that has garnered increasing concern in recent years is the use of a specific class of pesticides, organophosphates (OPs).

## OBJECTIVE

The objective of this review is to summarize the various correlations and associations demonstrated in recent scientific literature between long-term exposure of OP's and the development of human metabolic diseases, including their potential mechanisms. The specific OPs considered in this review are chlorpyrifos, diazinon, trichlorfon, coumaphous, dichlorvos, phorate, malathion, and terbufos.

## METHODS

Articles published between 2007 and June 2018 describing the association between OPs and the development of obesity, T2DM, and metabolic syndrome were included in this review.

## RESULTS

This review of scientific literature from 2007-2018 showcased multiple correlations and associations between chronic/sub-chronic exposure to OPs and the development of obesity, T2DM, and metabolic syndrome. Induction of insulin resistance, elevated oxidative stress, dysregulation of lipid metabolism, and alteration of gut microbiota were proposed mechanisms by which OPs increased susceptibility to metabolic diseases.

## CONCLUSION

Chronic exposure to organophosphates leads to increased susceptibility of metabolic diseases. To explore the association between chronic OP exposure and the incidence of metabolic diseases, better methods for the analysis and detection of OPs at low concentrations in human tissues are critically needed. The data obtained could serve as the foundation in the development of human health risk assessment and regulatory guidelines as it pertains to OP exposure and metabolic diseases.

# **SURVIVAL OUTCOMES FOR STAGE I NON-SMALL CELL LUNG CANCER (NSCLC) PATIENTS WITH POSITIVE TUMOR MUTATIONS FOUND VIA LIQUID BIOPSY**

**FREEZE, MEGAN, TERESA PARENT, RN, MARK BOWLING, MD, HYDER ARASTU, MD, PAUL WALKER, MD, AND ANDREW JU, MD**

## **BACKGROUND**

The nature of cancer is when normally functioning cells mutate to allow for unmitigated growth, invasion, and metastasis. These mutations can act as indicators for optimal treatments and prognosis (Owada-Ozaki). Tumor mutations are usually determined by solid tumor biopsy. However, some tumors are unable to be biopsied due to location or patient comorbidity. It has been recently shown that cancer patients have circulating tumor cells in the blood stream, even as early as Stage I (Hanssen A). These can be tested for common cancer mutations. This is particularly interesting for patients treated with Stereotactic Body Radiation Therapy (SBRT), as they are generally inoperable, making liquid biopsy of particular interest given the relative paucity of cells for other mutational analysis.

## **OBJECTIVE**

We hypothesized in this study that survival outcomes for Stage I Non-small Cell Lung Cancer (NSCLC) patients treated with SBRT who are positive for liquid biopsy tumor mutations would be different than those in patients whose tumor mutations were not detected via liquid biopsy.

## **METHODS**

This was a retrospective review of a cohort of patients who have had liquid biopsy and been treated with SBRT for Stage I NSCLC. Outcomes were measured by patient survival and PERCIST response. Analysis of the data was conducted using Kaplan-Meier survival curves with a log rank test. Analysis of PERCIST response was conducted with a Chi-squared test. We followed 41 primary tumors among 34 patients diagnosed with stage I NSCLC.

## **RESULTS**

Results revealed that there was no statistically significant difference in survival ( $P = 0.2971$ ) and in PERCIST values ( $P = 0.1982$ ) between those patients positive for liquid biomarkers and those who tested negative. We hope to continue to explore this hypothesis further as we believe a larger group of patients meeting their endpoint is needed to provide more robust data. We would also like to investigate other clinical factors which could influence patient survival.

## **CONCLUSION**

We anticipate this data and the data collected from our expanded second iteration of this study, if shown to be a valid prognostic or therapeutic indicator, to eventually influence the pattern of treatment for patients living in eastern North Carolina.

# UNDERSTANDING THE EFFECTS OF ARRABIDAEA CHICA EXTRACT ON INFLAMMATORY SIGNALING PATHWAYS

WALTON GODWIN, WESLEY SHAW, MARY ANN FOGGIO, RAMIRO MURATA

---

## BACKGROUND

Oral mucositis is the painful inflammation and ulceration of oral tissues as a side-effect of aggressive cancer therapies such as radiotherapy or chemotherapy. Currently there is no treatment or cure for mucositis and the only relief available to patients is pain management. *Arrabidaea chica*, popularly known as Crajiru, has been traditionally used as wound healing agent for its anti-inflammatory properties. These properties can be utilized in the treatment of oral mucositis.

## OBJECTIVE

Investigate the effects of *A. chica* extract on Lipopolysaccharide and Zymosan initiated inflammatory pathways.

## METHODS

Human gingival fibroblasts (HGF-1, ATCC CRL-2014) were cultured in DMEM-5% FBS media at 37°C in 5% CO<sub>2</sub>. The cytotoxicity of *A. chica* extract on HGF was determined by 24-hour exposure of cells seeded in 96-well plate ( $1 \times 10^5$  cells/mL) at concentrations from 0.025-250 µg/mL. CellTiter-Blue cell viability assays were then performed to determine the LD50. HGF were exposed to stimulating concentrations of LPS and/or Zymosan PAMPs with or without *A. chica* extract. Sample supernatants and RNA were collected from samples at 0, 6, and 12-hour time points. Cytokine production was determined by Luminex analysis of the supernatants and RT-PCR performed on the RNA.

## RESULTS

CellTiter-Blue assays determined that *A. chica* extract is not toxic to HGF cells in low concentrations (LD50= 50 µg/mL). Luminex assays indicated that cells exposed to *A. chica* extract express lower amounts of cytokines when exposed to LPS or Zymosan than cells without extract.

## CONCLUSION

*Arrabidaea chica* extract may inhibit cytokine expression in human gingival fibroblasts after exposure to LPS or Zymosan. Additional research is needed to accurately determine where in the inflammatory pathway the extract is interfering.



# COMPREHENSIVE PATIENT INTAKE INFORMATION FORM IMPROVES OUTPATIENT WOUND-CENTER PATIENT CARE

SPENCER M. JACKSON AND CLINTON E. FAULK, MD

---

## BACKGROUND

Increased prevalence of chronic wounds in an aging population has led to astronomical increases in health care costs. Wound etiology is often multifactorial, yet patients rarely present with identical medical complications or comorbidities, adding more time to diagnosis and increasing likelihood of a decline in patient health and decreased wound healing. Patient intake plays a crucial role at the front lines of medical care. We identified in our outpatient wound center, a need to change the methodology of patient intake to provide better point-of-care and improve center efficiency.

## OBJECTIVE

An expanded and comprehensive patient intake form, specific to our patient population, may improve the care of both acute and chronic wound care patients in our outpatient wound care center.

## METHODS

Our methodology included a literature review describing multiple comorbidities that negatively impact wound healing processes. We also designed a new system to present wound size and location. Lastly, the five most common wounds were identified in our clinic and associated with their most common comorbidities.

## RESULTS

Upon review of the literature, we identified several comorbidities not previously included on our patient intake form. These are as follows: kidney disease, spinal cord injuries, lymphedema, rheumatoid arthritis, peripheral vascular disease, deep vein thrombosis, and sickle cell disease. The most common presenting wound types were venous stasis ulcer, arterial ulcer, diabetic foot ulcer, pressure ulcer, and traumatic wound. A diagram was formatted allowing patients and providers to shade specific and or multiple wound locations. General intake questions were formulated pertaining to ambulatory status, residence, transportation type, and decision-making capacity.

## CONCLUSION

By redesigning our wound care patient intake form, we were more able to accurately schedule patients, which increased center efficiency. Many patients may need longer appointment intervals than the previous standard of 15 minutes, especially those with ambulatory and transportation complications.

# THE ASSOCIATION BETWEEN PREGNANCY EXPOSURES WITH FETAL METABOLITES AND NEONATAL OUTCOMES

GABRIELLE KATTAN, DEVON KUEHN, M.D., SRIKANTH RAVISANKAR, M.D.

---

## BACKGROUND

Neonatal Abstinence Syndrome (NAS) is an array of signs and symptoms experienced by a newborn after birth due to abrupt discontinuation of intrauterine drug exposure. Current challenges in the hospital include determining which neonates will develop NAS, if the neonate will require morphine sulfate therapy, or the duration of neonatal hospital stay. Studies correlating maternal substance dose and standard of care meconium analysis have failed to demonstrate any significant relationships between maternal opioid dose, meconium concentrations of methadone, and neonatal outcomes. It has been hypothesized that maternal drug dose and meconium levels are not reflective of true fetal exposure levels.

## OBJECTIVE

The primary aim of the study is to determine the association between quantified opioid exposure and its metabolites (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), 2-ethyl-5-methyl-3,3-diphenylpyrrolidine (EMDP) and methadone) on key nutrients in pregnancy and neonatal outcomes.

## METHODS

A single-center, prospective, case-control study with enrollment limited to control (no illicit drug, alcohol or nicotine exposure) or opioid-dependent and/or known polysubstance use, singleton pregnant women with a gestational age  $\geq 34$  weeks who are admitted to Vidant Medical Center (VMC) Labor and Delivery Unit in labor. 50 controls, 50 opioid-dependent mothers (targeting 20 without polysubstance use (to include nicotine), and 50 marijuana-only using mothers will be approached in total. Patient demographics, infectious history, drug use and delivery data will be abstracted from the chart. The mother will be asked to complete two surveys: a food frequency questionnaire (FFQ) to assess the nutritional status during the pregnancy and the modifiable physical activity questionnaire (MPAQ).

## RESULTS

As of July 2018, a total of 93 patients have been approached with 52 consented for study participation. The total number of patients in each category are: 28 controls, 14 polysubstance abuse, 5 opioid-dependent, and 13 marijuana exposed patients.

## CONCLUSION

Further recruitment of patients and data analysis will be completed. Upon study completion, regression analysis will be completed to determine the association between umbilical cord and umbilical cord blood LC/MS opioid results and neonatal outcomes.

# MALNUTRITION AND THE NEED FOR INCREASED HEALTHCARE IN SOLOLÁ, GUATEMALA

**KRAGEL, EA, BRODY SCHOOL OF MEDICINE; FLOOD, DMN, BRODY SCHOOL OF MEDICINE;  
HAVEN, KE, BRODY SCHOOL OF MEDICINE DEPARTMENT OF FAMILY MEDICINE**

## **BACKGROUND**

Malnutrition is one of the many diseases that has an increased burden in the Indigenous population in Guatemala, with approximately 80% of Indigenous children being chronically malnourished.

## **METHODS**

Community interviews, N=84, were conducted in four communities in Sololá, Guatemala. Height-for-age measurements of children under 5 were taken to assess stunting prevalence and determine relative burden of malnutrition. Mothers with children under the age of 5 responded to study measures concerning factors that might contribute to the prevalence of malnutrition in the various communities. The following factors were assessed: nutritional intake, risk of high infectious disease burden, prenatal care, and breastfeeding.

## **RESULTS**

Data was analyzed to determine which factors were more associated with malnutrition. The only factor that was significantly associated with stunting was nutritional intake, OR= 16.5,  $p=0.014$ . Inadequate nutritional intake correctly predicted 71% of cases of stunting in the sample. Additionally, stunting increased odds of high rates of self-report illness per month, OR= 4.8,  $p=0.015$ .

## **CONCLUSION**

This data was presented to and shared with the community partner, a local doctor at a nonprofit, free clinic. The results of the research are being applied to direct an intervention in these communities to reduce the burden of malnutrition. Height-for-age measurements will be utilized as baseline data to gauge effectiveness of future interventions.

# LAPAROSCOPIC HIATAL HERNIA REPAIR WITH ESOPHAGEAL SPHINCTER MAGNETIC AUGMENTATION AND GASTROPEXY FOR GASTROESOPHAGEAL REFLUX DISEASE PROVIDES SIMILAR SAFE POST-OPERATIVE OUTCOMES AS WITHOUT GASTROPEXY

ETHAN LEDBETTER, JAMES SPEICHER, MD, ANTHONY MOZER, MD, LUKE HUNTER, CARLOS ANCIANO, MD

## BACKGROUND

For several years, a magnetic lower esophageal sphincter augmentation (MSA) device called LINX has been used to surgically treat acid reflux symptoms in patients who also have a hiatal hernia (HH). Thus far, published literature on the success of LINX on patients with hiatal hernias greater than 4.0 cm has been minimal. We sought to determine the effectiveness and safety of LINX with a gastropexy (PLINX) on patients with hernias greater than 4.0 cm transverse crural diameter (TCD) or other high-risk factors for hernia recurrence (HRHR).

## OBJECTIVE

Patients with hiatal hernias greater than 4.0 cm TCD or HRHR who underwent PLINX procedure will have similar post-operative gastroesophageal reflux disease (GERD) outcomes as patients who underwent LINX procedure without gastropexy.

## METHODS

A retrospective chart review of 75 patients who underwent MSA implantation was performed. Post-operative GERD outcomes such as resolved symptoms, dysphagia, discontinued use of proton pump inhibitor (PPI) in absence of other indication, and esophagogastroduodenoscopy / dilation procedures were compared between groups of patients who underwent the LINX procedure with or without gastropexy. Other variables such as age, BMI, gender, esophageal dysmotility scores, acid reflux scores, and co-morbidities were also recorded to observe similarities between the two groups.

## RESULTS

39 patients underwent the LINX procedure without gastropexy and 36 patients underwent the PLINX procedure. Groups experienced equal amounts of dysphagia ( $p = .098$ ), underwent the same number of post-operative EGD dilations ( $p = .156$ ), and had equal number of patients who continued PPI use post-operatively ( $p = .433$ ). One patient from the non-gastropexy group reported unresolved GERD symptoms solely while no patients from the PLINX group reported unresolved symptoms ( $p = 1.000$ ). No HH recurrences occurred in either group.

## CONCLUSION

PLINX procedure appears similar in safety and effectiveness in comparison to HH repair and MSA when treating patients with GERD and hiatal hernias greater than 4.0 cm or HRHR. Further studies that include quantitative patient quality of life assessments and long-term follow-up evaluations should be considered to further validate the PLINX procedure.

# DOPAMINE MODULATORS RESTORE MORPHINE EFFICACY AND PREVENT THE DEVELOPMENT OF MORPHINE TOLERANCE IN RATS

SZU-AUN LIM, HELEN RODGERS, JACOB YOW, STEPHEN CLEMENS, KORI BREWER

## BACKGROUND

Chronic neuropathic pain is a common, debilitating consequence of spinal cord injury (SCI). Current pharmacological treatment options include opioids, such as morphine, which are often ineffective for long-term therapeutic use due to the emergence of tolerance and dependence. Previous studies show that dopamine modulators can acutely enhance the analgesic effects of morphine. However, the acute analgesic effects of dopamine modulators in a neuropathic pain model and its implication on tolerance and dependence are unknown.

## OBJECTIVE

To demonstrate that the combination of either a D1-receptor antagonist (SCH39166) or a D3-receptor agonist (pramipexole) in combination with morphine increases the analgesic efficacy of morphine and prevents the development of morphine tolerance and dependence rats.

## METHODS

Acute analgesia: Mechanical and thermal thresholds were assessed through von-Frey and tail-flick in adult, female Long-Evans rats at 21-30 days post-contusion SCI, sham surgery, or in uninjured controls. Baseline thresholds were compared to thresholds following administration of drug conditions: (1) saline, (2) morphine, (3) morphine+SCH39166, (4) morphine+pramipexole, (5) SCH39166, (6) pramipexole. Morphine tolerance: Uninjured controls received continuous delivery of drug conditions (1)-(4) through osmotic pumps for 14 days. Thresholds were measured following acute morphine challenges at days 7 and 14 and compared to baseline thresholds (day 0). Dependence: Uninjured controls were assessed for withdrawal signs for at 48 and 72 hours following pump removal.

## RESULTS

Acute analgesia: Contusion SCI resulted in animals that were morphine resistant. Adjuvant treatment with pramipexole or SCH39166 improved morphine analgesia in SCI animals as indicated by an increase in mechanical and thermal thresholds. Morphine tolerance: Morphine failed to provide analgesia after 14 days of chronic morphine exposure as indicated by a significant reduction in both mechanical and thermal thresholds vs. baseline. Chronic exposure to the combination conditions did not result in a loss of morphine analgesia over 14 days. Dependence: The addition of pramipexole or SCH39166 did not induce dependence at dosage tested.

## CONCLUSION

The addition of dopamine modulators restores the effectiveness of morphine and prevents the emergence of morphine tolerance. This data provides support for a novel clinical intervention for patients whose pain is unresponsive to morphine alone.



# MECHANISMS UNDERLYING PERMANENCE OR REMITTANCE OF KATP-INDUCED NEONATAL DIABETES

**WILLIAM H. MCALLISTER (BRODY SCHOOL OF MEDICINE, EAST CAROLINA UNIVERSITY), CHRISTOPHER H. EMFINGER AND MARIA S. REMEDI, WASHINGTON UNIVERSITY IN ST. LOUIS**

## BACKGROUND

Gain of function (GOF) mutations in the ATP-sensitive potassium (KATP) channels cause human neonatal diabetes mellitus (NDM) due to interruption of glucose-dependent insulin secretion. When KATP -GOF mutation induced mice are treated with the sulfonylurea glibenclamide for a short period of time at disease onset, some mice, as expected, remain diabetic after treatment ended (non-remitters), while others showed relatively normalized blood glucose levels (remitters). Previous analysis of KATP -GOF remitter and non-remitter mice has shown differences in insulin sensitivity long after treatment ended suggesting changes in sensitivity are a consequence and not a cause of remittance. Inflammatory cytokines, IL-6 and TNF-alpha, significantly differed between remitter and non-remitter mice before and during diabetes induction.

## OBJECTIVE

To further exam possible differences in inflammatory cytokines and basal insulin secretion as driving factors in NDM remittance, fasting and fed blood samples were taken from KATP -GOF mice at days 0, 5, 14, and 35+.

## METHODS

RNA extracted from isolated islets was analyzed through quantitative real-time PCR and pancreatic paraffin sections were stained to look at alpha-cell and beta-cell identity.

## RESULTS

An ELISA for basal insulin levels revealed no significant differences in levels between groups. Immunological multiplex assay revealed that cytokines involved in NF-κB pathway had trends contrasting those observed in IL-6 and TNF-alpha. IP-10 levels showed increased levels in remitters compared to non-remitters, while IL-12 p40, MCP-1, and IFN-gamma had elevated levels in controls compared to remitters and non-remitters at various time points. Beta-cell representative gene expression for insulin and Nkx6.1 showed a trend of elevation relative to non-remitters. These results are supported by the stark decrease in non-remitter insulin staining and significant increase in glucagon positive cells compared to remitters, including infiltration of glucagon positive cells in the core of the islet. Despite the differences observed in several inflammatory cytokines between remitter and non-remitter mice mentioned above, preliminary data demonstrating increased remittance rates in KATP -GOF mice co-treated with the anti-inflammatory agent, meloxicam, suggest that certain cytokines play a crucial role in NDM progression.

## CONCLUSION

These results prompt us to further explore the role of inflammation and inflammatory cytokines as a mechanism underlying the remittance of NDM.

# ANTIBODY-MEDIATED TRAPPING OF HERPES SIMPLEX VIRUS IN CERVICOVAGINAL MUCUS

JUSTIN D. MCCALLEN; HOLLY A. SCHROEDER; ALISON SCHAEFER; SAMUEL K. LAI

## BACKGROUND

Antibodies and mucus are critical components in protecting against infection at mucosal surfaces. In the female genital tract, cervicovaginal mucus (CVM) acts as a physical and biochemical barrier to protect against sexually transmitted pathogens. IgG is the predominant immunoglobulin in CVM and diffuses through mucus to bind pathogens. We previously showed that antigen-specific IgG1 immobilized herpes simplex type 1 (HSV-1) in CVM. Virion immobilization was attributed to multiple low-affinity bonds between the array of bound IgG on individual virions and mucins, specifically mediated by N-glycans on the IgG Fc domain.

## OBJECTIVE

Immunoglobulin subclasses have variable Fc-domain structures and glycosylation that may impact antibody trapping potency in CVM. We hypothesize that these differences could impact Fc-glycan-mucin interactions and pathogen trapping potency in CVM.

## METHODS

We employed fluorescence microscopy with multiple particle tracking to quantify the mobility of fluorescent HSV-1 in 45 CVM specimens treated with 5 ug/mL anti-HSV-1 antibody (IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2) or non-specific IgG. To validate whether Ab Fc-glycan was required for trapping by all isotypes, antibodies were deglycosylated with PNGaseF and their trapping potency was compared to their native counterpart. Additionally, antibody binding affinity to virus, endogenous anti-HSV-1 IgG, and lactic acid levels in CVM supernatants were quantified via ELISA.

## RESULTS

Two groups of CVM specimens emerged: those where all native anti-HSV-1 isotypes trapped (Trappers) and those where no mAbs trapped virus (Non-trappers). Among trappers, all isotypes were significantly different from control ( $p < 0.05$ ). Unexpectedly, only IgG1 trapped more effectively than their deglycosylated counterparts. To explain these results, we compared native and deglycosylated antibody affinity to HSV-1 and observed no differences. Furthermore, we found no correlation between HSV-1 mobility and endogenous anti-HSV IgG for any isotype. Finally, we measured the D-lactic acid and L-lactic acid as indirect indicators of vaginal microbiome health, and observed no correlation between virus mobility and lactic acid content.

## CONCLUSION

These findings underscore the ability for antibodies to reinforce the mucosal barrier against foreign pathogens. While the results of this study require further investigation to elucidate interspecimen variability in anti-HSV-1 trapping, this study informs the design of vaccine or passive immunization strategies to induce antibody subclasses that maximize protection against mucosal transmission of infectious viruses in the female reproductive tract.

# QUALITATIVE ANALYSIS OF ORAL HEALTH STATUS AMONG PATIENTS WITH MENTAL ILLNESS AND ASSOCIATED BARRIERS AS PERCEIVED BY PSYCHIATRIC PATIENTS AND DENTAL PROVIDERS

JONATHAN NOWLIN, JOSEPH LEE, PAIGE AVERETT, VIVEK ANAND, JANET BENJAMIN, AND WANDA WRIGHT

---

## BACKGROUND

Mental illness (MI) correlates with poor oral health outcomes. With 1 in 5 people in the United States living with a mental health condition, there is a significant portion of the population at an increased risk of dental disease.

## OBJECTIVE

The aim of this qualitative study was to assess the attitudes and experiences of both dentists and psychiatric patients and compare their perceptions of barriers to oral health care faced by patients with MI.

## METHODS

Dentists at East Carolina University (ECU) School of Dental Medicine and psychiatric patients of ECU Outpatient Psychiatry Center were purposively sampled for a qualitative study. Participating dentists (n=25) and psychiatric patients (n=20) underwent a 15-minute semi-structured interview. The interviews were recorded, transcribed, and thematically coded via grounded theory analysis.

## RESULTS

Three key themes emerged from the dental faculty interviews: (1) the need for interprofessional collaboration, (2) additional training and educational initiatives, and (3) barriers to oral health care. In addition, four key barriers to oral health care emerged from the psychiatric patient interviews: (1) socioeconomic limitations, (2) dental fear/anxiety, (3) lack of motivation, and (4) embarrassment. All of the barriers reported by the psychiatric patients were consistent with the barriers to oral health care mentioned by the dental providers, with the exception of feelings of embarrassment caused by poor oral health status.

## CONCLUSION

Our findings highlight the need to address the barriers inhibiting the patient population with MI from seeking more oral care. Dental anxiety and fear were reported by the psychiatric patients as leading causes of dental care avoidance, resulting in some patients avoiding the dentist for over ten years. We feel this can be improved by increasing interdisciplinary communication between dentists and psychiatrists, in addition to training dentists to manage the source of the patient's dental anxiety and fear to ensure that they are comfortable and willing to continue to seek regular dental care in the future.

# **HYPERCALCEMIA DUE TO PRIMARY HYPERPARATHYROIDISM PRESENTING WITH DEPRESSION AND NON-SPECIFIC SOMATIC FEATURES: A BROAD DIFFERENTIAL DIAGNOSIS IS ESSENTIAL TO EARLY DIAGNOSIS**

**SHIVAM P. PATEL, B.S., SIERRA R. BOSTIC, PHILIP J. BOYER, M.D., PH.D.**

---

## **BACKGROUND**

Hypercalcemia can be seen as (1) a primary process, most often due to a parathyroid adenoma, or (2) a secondary process, e.g. due to a paraneoplastic secretion of parathyroid hormone-related peptide by a neoplasm such as squamous cell carcinoma. Hypercalcemia can affect multiple organ systems and manifest clinically with a wide variety of symptoms: neurologic/psychiatric, skeletal, renal, gastrointestinal, and cardiovascular and early diagnosis can be challenging and delayed.

## **OBJECTIVE**

We describe in a retrospective case report an individual presenting with non-specific clinical features who was ultimately diagnosed with primary hypercalcemia 6 months after initial presentation. A literature search including key words hypercalcemia and hypercalcemia was undertaken and pathology, internal medicine text books, and peer-reviewed online resources including UpToDate.com were queried.

## **RESULTS**

A 20-year-old woman presented with listlessness and a reduced energy level consistent with depression. She subsequently experienced right flank pain and passed a stone (nephrolith) in her urine; it was not analyzed. A serum metabolic screen identified a calcium level of 11.0 mg/dL (reference range: 8.4 - 10.2 mg/dL). Further workup included serum parathyroid hormone evaluation (206 pg/mL; reference range: 12 - 88 pg/mL), ultrasound examination of the neck, and a sestamibi scan, which identified an enlarged, hypermetabolic right inferior parathyroid gland while other parathyroids were normal in size and normo- or hypometabolic. Resection was undertaken, confirming parathyroid cell proliferation, consistent with a parathyroid adenoma. Serum calcium and parathyroid hormone levels returned to the normal range (9.4 mg/dL and 36 pg/mL, respectively) and symptoms resolved within 1-2 weeks. Literature, textbooks, and online resources cite the challenges to the early diagnosis of hypercalcemia particularly in the setting of non-specific psychiatric symptoms.

## **CONCLUSION**

Given the range of presentations, the diagnosis of hypercalcemia can be significantly delayed and lead to significant complications. A broad differential diagnosis including consideration of toxic-metabolic-nutritional etiologic processes including hypercalcemia is essential as the student and physician consider disease processes which may affect one or multiple organ systems. An expanded metabolic screen, including total calcium determination, must be performed. This case report characterizes the difficulty in making the clinical diagnosis of hypercalcemia.

# RETROSPECTIVE APPLICATION OF THE MODIFIED EARLY WARNING SCORE (MEWS) TO PATIENT SURVIVAL AT VIDANT MEDICAL CENTER

SHIVAM P. PATEL, MSII, KORI L. BREWER, PHD, ANTHONY J. FRANK, JR., MD, MBA, FACEP

## BACKGROUND

The Modified Early Warning Score (MEWS) is a physiological scoring system calculated based on the following vital signs: body temperature, heart rate, respiratory rate, and systolic blood pressure. The MEWS system, specifically heart rate and respiratory rate, has previously been observed to indicate the need for Emergency Response Team (ERT) activation, but it has not been studied as an indicator of survival.

## OBJECTIVE

We hypothesized that the MEWS system could serve as a predictor of patient survival.

## METHODS

To investigate this possibility, the MEWS system was retrospectively applied to 165 ERT activations at Vidant Medical Center. Based on an established scoring scale for each vital sign, MEWS measurements were calculated for each patient at multiple time points pre-ERT activation and during ERT activation. Additionally, it was determined whether the patient survived his or her hospital stay during which the ERT was activated. Paired t-test analysis was used to determine associations between the four MEWS criteria and survival.

## RESULTS

Overall, MEWS values significantly increased from 6 hours before ERT activation until ERT activation for both the group of patients who survived ( $p < 0.001$ ) and the group of patients who did not survive ( $p = 0.04$ ). Changes in both heart rate and respiratory rate from 6 hours before ERT activation until ERT activation were significantly associated with increased MEWS values for the patients who survived ( $p = 0.03$ ). Changes in respiratory rate alone from 6 hours before ERT activation until ERT activation were significantly associated with increased MEWS values for the patients who did not survive ( $p < 0.001$ ).

## CONCLUSION

These results confirm previous findings, which suggested that changes in heart rate and respiratory rate may alter MEWS more notably than changes in body temperature or systolic blood pressure. These data also indicate that respiratory rate may need to be weighed greater than the other three measures of the MEWS system, as it was the only vital sign to significantly change the MEWS measurement in the population of patients who did not survive.

# IFN- $\beta$ STABILIZES A NOVEL SUBSET OF 'DOUBLE-POSITIVE' CD4+ CD8+ FOXP3+ REGULATORY T CELLS

PRUITT Z, MD MANNIE, S PERRY, AND D GHOSH

## BACKGROUND

IFN- $\beta$  is an immunomodulatory type I interferon used as a therapy for Multiple Sclerosis (MS). However, the mechanism by which IFN- $\beta$  mediates therapeutic activity in MS is unknown. Several lines of indirect evidence suggested that IFN- $\beta$  may drive the differentiation of immunosuppressive FOXP3+ regulatory T cells (Tregs) and that this mechanism may account for the therapeutic action of IFN- $\beta$  in MS.

## OBJECTIVE

The objective of this study was to test the novel hypothesis that high concentrations of IFN- $\beta$  induced and stabilized CD4+ CD25+ FOXP3+ Tregs. Also, we predicted that IFN- $\beta$  would effectively induce and stabilize a specialized CD8+ lineage of CD4+ Tregs.

## METHODS

To evaluate the inductive activity of IFN- $\beta$ , FOXP3-reporter wildtype CD4+ T cells were cultured with or without 2.5  $\mu\text{g/ml}$  Con-A in the presence or absence of 10 nM TGF- $\beta$ , 1  $\mu\text{M}$  IFN- $\beta$  or both. Control wells included 0.5% IL-2 + 10  $\mu\text{g/mL}$  PC61 (anti-IL2RA mAb). Following a 3-day culture, cells were stained with fluorochrome-conjugated antibodies and were analyzed with a LSRII Flow Cytometer and FloJo Software.

## RESULTS

CD4+ T Cells exposed to 1  $\mu\text{M}$  IFN- $\beta$  exhibited a CD4+ FOXP3+ phenotype, while control T cells exhibited baseline Treg percentages ( $20.3 \pm 0.3\%$  versus  $4.4 \pm 0.6\%$ , respectively). A replicate experiment revealed that  $27.8 \pm 1.5\%$  and  $17.9 \pm 0.9\%$  of CD4+ T cells became Tregs when exposed to 1  $\mu\text{M}$  IFN- $\beta$  and 10 nM IFN- $\beta$ , respectively. Also, 1  $\mu\text{M}$  IFN- $\beta$  maintained 27.1% CD4+ CD8+ Tregs compared to baseline levels (19.3%). This project thereby revealed that IFN- $\beta$  induced and stabilized a novel lineage of CD4+ CD8+ FOXP3+ Tregs.

## CONCLUSION

IFN- $\beta$  was shown to induce and/or stabilize the CD4+ CD8+ FOXP3+ Treg subset. IFN- $\beta$  has potential for use as a therapeutic reagent to induce and maintain expanded populations of CD4+ CD8+ Tregs. This discovery opens numerous avenues for future investigation regarding the intersection of IFN- $\beta$  and Treg biology.



# EX VIVO RADIATION INHIBITS NEURITE OUTGROWTH IN DISSOCIATED VERSUS WHOLE MAJOR PELVIC GANGLIA CULTURE

JOSHUA T. RANDOLPH, ELENA PAK, JOHANNA L. HANNAN

---

## BACKGROUND

Prostatic radiation therapy causes nerve damage to pelvic ganglia resulting in erectile dysfunction (ED). In rodents, the major pelvic ganglion (MPG) is a correlate to the hypogastric plexus and is used to study neurogenic ED. The effect of radiation on neuronal survival and growth within the MPG is unknown. This study will also assess differences between irradiated MPGs grown in dissociated vs organotypic culture.

## OBJECTIVE

We hypothesized that radiation will result in increased neuronal apoptosis and decreased nitrergic neurons in dissociated MPG culture. Additionally, a reduction in neurite growth will be seen in both dissociated and organotypic MPG culture.

## METHODS

MPGs from male Sprague-Dawley rats (n=10) were removed and irradiated ex vivo (0 or 800cGy). For dissociated culture, MPGs were digested in collagenase/dispase and neurons cultured on coverslips for 72 hours. Immunofluorescent staining for class III beta-tubulin (neuron-specific), neuronal nitric oxide synthase (nNOS; nitrergic marker), tyrosine hydroxylase (TH; sympathetic marker), and TUNEL was performed to assess neurite length, branching and apoptosis. For organotypic culture, whole MPGs were grown in Matrigel and neurite growth was measured at 24, 48, and 72 hours. For both methods, images were taken at 100x magnification and neurite length was measured using Image J.

## RESULTS

Irradiated MPGs grown in dissociated culture demonstrated less neurite outgrowth ( $p < 0.01$ ) and no change in neurite branching. Apoptosis was markedly increased in irradiated dissociated neurons ( $p < 0.001$ ). The prevalence of nNOS+ and TH+ neurons were unchanged in irradiated dissociated culture. In organotypic culture, irradiated MPGs demonstrated increased neurite outgrowth at 24 and 48 hours ( $p < 0.05$ ). However, at 72 hours, there was no difference in neurite length. When comparing neurite growth between the two culture methods at 72 hours, the dissociated neurons were 22% shorter while neurites from irradiated whole MPGs were 15% longer ( $p < 0.01$ ).

## CONCLUSION

MPG neurite growth was inhibited in irradiated MPGs grown as dissociated neurons, but not in organotypic culture. Schwann cells are known to facilitate repair of damaged neurons, and may be providing a neurotrophic environment for radiated neurons in the intact MPG. Future studies will examine the transcriptional expression of markers of apoptosis and activated Schwann cells in the radiated MPGs from organotypic culture, and the impact of co-culturing dissociated MPG neurons with Schwann cells.

# THE INFLUENCE OF PREDICTED MINUTE VENTILATION (MVPRED)-ESTIMATION METHODS ON POSTOPERATIVE HYPOVENTILATION PROFILES IN OBESE SURGICAL PATIENTS

FORREST ROBERSON, COLLEEN DINGMANN, ANA FERNANDEZ-BUSTAMANTE

## BACKGROUND

Impedance-based noninvasive respiratory volume monitors (RVMs) provide a continuous assessment of tidal volume, respiratory rate, and minute ventilation (MV), and they can alert providers to hypoventilation events before hypoxemia develops. Hypoventilation events can be defined as  $MV < 40\%$  of predicted MV ( $MV_{pred}$ ) for that patient for greater than or equal to 1 minute. However, the  $MV_{pred}$  for each patient can be calculated using their predicted body weight (PBW) or a variety of formulas to estimate body surface area (BSA), as recommended for obese patients.

## OBJECTIVE

We hypothesized that the duration (minutes) of hypoventilation in our group of bariatric surgery patients would be different depending on the  $MV_{pred}$ -estimation method used.

## METHODS

Patients were selected from an ongoing study enrolling bariatric surgery patients. Patients were monitored throughout surgery and PACU with the RVM ExSpirom (Respiratory Motion, Inc.) device. Upon discharge from PACU, MV data was exported. The events of averaged  $MV < 40\%$   $MV_{pred}$  for greater than or equal to 1 minute, and their duration (per event and total accumulated minutes), were calculated using the PBW method, Mosteller BSA calculation and DuBouis & DuBois (D&D) methods. We compared the number of events and total accumulated minutes of hypoventilation between the 3 methods. Relevant clinical data during the PACU stay were also collected from the electronic medical record.

## RESULTS

Seven patients were included in this analysis. Only one patient presented no postoperative hypoventilation consistently across the three methods. At least one hypoventilation event was observed in 6 patients. In 2 of these patients the events were undetected by the PBW  $MV_{pred}$ -estimation method, though they had 1-8 events with the BSA methods. In the 6 patients with observed hypoventilation, the total episodes of hypoventilation ranged from 1 to 15 events and the accumulated hypoventilation minutes from 1 to 73 minutes. The PBW  $MV_{pred}$ -estimation method resulted in the lowest number of hypoventilation events and minutes and the Mosteller BSA  $MV_{pred}$ -estimation method the highest.

## CONCLUSION

Hypoventilation events in the PACU were common in this subset of obese patients after bariatric surgery. The 3 methods can be used to determine hypoventilation events but the frequency and duration (minutes) varied widely depending on the method used.

# HAVE THE RECENT CHANGES IN DCB REIMBURSEMENT AFFECTED PAD PATIENT CARE? - A SINGLE CENTER EXPERIENCE

ARTHUR M. SAMIA, IVY C. SMITH, PAUL STRONG, GEORGE L. ADAMS

## BACKGROUND

Balloon angioplasty (BA) and stenting have long been the mainstays of endovascular therapy in peripheral arterial disease (PAD). However, in recent years, the rise of drug coated balloons (DCBs) has revolutionized care, with multiple clinical trials showing superiority over BA in maintaining primary patency and freedom from target lesion revascularization (TLR). With the recent drop of the add-on payment for DCBs, a barrier for their use and consequently reduced therapy adoption in PAD might arise. It will be important to assess if this could indeed affect the behavior of physicians and hospital administration towards stocking and using DCBs.

## METHODS

This single center, retrospective study looks at DCB utilization in 2017 versus 2018. Data has been collected in two groups: 1) July 1, 2017 to December 31, 2017 – with pass through code (PTC) – prior medical billing reimbursement – and 2) January 1, 2018 to June 30, 2018 – without PTC – markedly reduced reimbursement. Included were patients that were treated for superficial femoral artery (SFA) or popliteal artery (POP) disease. The study aims to determine changes in DCB utilization between the years with and without PTC. Furthermore, we will investigate treatments that have replaced DCBs. In addition, we aim to collect data on readmissions and procedure cost compared to national data.

## RESULTS

From July through December 2017, 350 DCBs were used in 209 patients (~1.675 DCBs/patient), while from January through June 256 DCBs were used in 180 patients (~1.422 DCBs/patient) – a 15.07% reduction in DCBs per patient. In addition, we will present the detailed numbers of DCB treated patients as fractions of total interventions in the group without PTC versus with PTC. Next steps in data analysis will determine if this shift is owed to other treatment strategies such as BA, atherectomy + BA, BA + bare metal stent, or BA + drug eluting stent.

## CONCLUSION

In a world increasingly focused on the value of care, this study is a first step to understand the possible impact of DCB reimbursement changes on their utilization in PAD. Furthermore, it will give an idea if, and how, these changes affect procedural cost and outcomes for patients.

# HIGHER PEEP VALUES DURING SPONTANEOUS BREATHING TRIALS INCREASE LIKELIHOOD OF SUCCESSFUL EXTUBATION IN OBESE PATIENTS

DEREK SCHAAP, JENNIFER STAHL, BRYAN GERBER, MANUEL IZQUIERDO

---

## BACKGROUND

Extubation of patients from mechanical ventilation in the Intensive Care Unit (ICU) can be a complex and often unpredictable decision that must be made, and failed attempts occurring in up to 20% of these patients are directly associated with increased morbidity. Excessive work of breathing is a major cause of these failures and breathing trials have since been established to help predict extubation success<sup>1</sup>. Given the altered physiology of obese individuals, increased work of breathing is a more prevalent issue and is compounded by a lack of literature for guidance in this population, further complicating the decision of extubation.

## OBJECTIVE

We hypothesize that obese patients utilizing higher PEEP (Positive End Expiratory Pressure) values during Spontaneous Breathing Trials (SBT) will lead to higher rates of extubation success.

## METHODS

1,796 medical records from all obese patients (BMI > 35 or weight > 250lbs.) 18 years of age or older who were treated in the ICU at Vidant Medical Center from January 1st, 2009 to present were retrospectively reviewed to obtain data about mechanical ventilator settings, results of SBTs, extubation outcomes, and patients' clinical courses. The cumulative review of this data will help determine if there is an optimal PEEP value that provides a more physiologic state to the patient and therefore a useful predictor of extubation success. This has the potential to significantly decrease the likelihood of failed attempts at extubation as well as its subsequent increase in morbidity.

## RESULTS

Analysis of the collected data is currently pending.

# **CYTOKINE PROFILE OF HUMAN GINGIVAL FIBROBLASTS FOLLOWING EXPOSURE TO LIPOPOLYSACCHARIDE AND ZYMOBAN PRESENT IN CELL WALL OF MICROORGANISM**

**WESLEY SHAW, WALTON GODWIN, DR. CATALINA GAY, DR. RAMIRO MURATA**

---

## **BACKGROUND**

Periodontal disease is a multifaceted disease that affects thousands, with a hallmark symptom of alveolar bone loss and loss of connective tissue attachment. The cause of periodontitis has been proven to be a result of the innate and adaptive immune response by cells and not the actual pathogens that are present. By studying how the cell reacts to LPS and Zymosan we can better understand the pathogenesis of periodontitis.

## **OBJECTIVE**

The objective of this study is to see how exposure to LPS and Zymosan effect Human Gingival Fibroblasts' immune response. Prior research has studied cytokine levels after exposure to both LPS and Zymosan. We aim to investigate the cells reaction to exposure to both LPS and Zymosan whether that be synergistic, antagonistic, or unchanged at varying time intervals. Exposure to both LPS and Zymosan will increase the production of cytokines while exposure to both will have the greatest effect. Zymosan will have a synergistic relationship with LPS and cytokine production will be at its maximum at 12 hours.

## **METHODS**

Human gingival fibroblasts (HGF-1) were expanded in T25 tissue culture flasks using 5% FBS DMEM medium. Cells were then plated in 24 plate wells. Cells were exposed to LPS, Zymosan, and both LPS and Zymosan for time intervals of 0, 6, and 12 hours. Following exposure, the RNA was extracted, and the cells' supernatant was collected. RT-PCR was conducted on the extracted RNA while Luminex was conducted on the supernatant. Western blot analysis was then conducted as well.

## **RESULTS**

There was a significant change in cytokine production when HGF cells were exposed to microorganisms.

## **CONCLUSION**

Exposure to both LPS and Zymosan increased the expression of the analyzed cytokines. Exposure to both LPS and Zymosan increased the expression at an even more drastic rate displaying a synergistic relationship between LPS and Zymosan.

# ASSESSING PRESSURE AND COERCION TO DONATE AMONG CANDIDATES FOR LIVING KIDNEY DONATION

JAMES E. STANTON, ANNIE ENO, ASHTON SHAFFER, MADELINE WALDRAM, ELIZABETH KING, MD, JEFFREY P. KAHN, PHD, LORI H. ERBY, PHD, JACQUELINE GARONZIK WANG, MD, MACEY HENDERSON, JD PHD, DORRY L. SÉGEV, MD PHD

---

## BACKGROUND

Transplant centers must ensure that living donors are not pressured to donate, especially as novel methods of identifying a living donor become more prevalent (e.g. use of social media, center-specific initiatives such as Live Donor Champion (LDC)).

## METHODS

Our center created and implemented a novel, 6-question pressure assessment for all potential living kidney donors since 11/2013. The pressure score was the average pressure reported on 5 Likert scale questions (1=least pressure, 5=most pressure). A sixth question assessed motivation for donation. Prior work retrospectively reviewed pressure assessments of 1,233 potential living organ donors from 11/25/2013-8/4/2015.

## RESULTS

Median (IQR) age of donor candidates was 43.1 (32.9-54.9), 62.9% were female, and 71.0% were white. Overall, 18.2% of potential donors had a pressure score >1. Pressure to donate was more often reported among males (21.6% vs. 16.2%;  $p=.02$ ), non-white potential donors (22.7% vs. 16.0%;  $p=.005$ ), and those related to their recipient (21.6% vs. 14.9%;  $p=.002$ ). An additional review and analysis of pressure assessments of 718 potential living organ donors from 11/25/2013-7/1/18 was conducted. Analysis for this data set is pending.

## CONCLUSION

This novel pressure assessment offers a way to identify pressured donor candidates early in the evaluation process.



# PHYSICAL ACTIVITY, NOT MATERNAL DIET, IS A SIGNIFICANT PREDICTOR OF DENTAL MATURITY AND INCIDENCE OF DENTAL CARIES IN OFFSPRING

SUMNER, BRANDEN, WINDLEY, TAYLOR, CURRENT J. LUKE, KORDIS, ALEX, MAY, LINDA

---

## BACKGROUND

The in utero environment provided by the mother during pregnancy influences the development of the fetus. Our previous findings demonstrate a statistical trend in tooth maturity and development as a function of the child's age related to maternal physical activity (PA) during pregnancy. In addition, nutrition while pregnant, especially foods high in polyunsaturated fatty acids (PUFA), has been associated with differences in child tooth development. It is unknown how maternal PA and nutrition during pregnancy interact to influence a child's tooth health and development.

## OBJECTIVE

The purpose of this study was to evaluate if diet during pregnancy modulates the influence of PA on the development of teeth of offspring. A secondary objective is to determine the influence of diet and exercise during pregnancy on dental caries of children.

## METHODS

Mothers with children, 6 years old and younger, who are patients of the ECU Pediatric Dental Clinic were recruited to participate in this study. Nutritional intake during the pregnancy was recorded through use of a Food Frequency Questionnaire. Based on the responses to a PA questionnaire related to the pregnancy, women were classified as exercisers, active, or control during their pregnancies. During these exams, Decayed, Missing, and Filled Surfaces and Decayed, Missing, and Filled Teeth were recorded. A total primary dentition count was taken in addition to a Caries Risk Assessment being recorded during the exam (AAPD). We utilized multiple ANOVAs and correlations to determine differences and associations of variables between groups, respectively. Regressions were used to determine which factor(s) was the best predictor of positive tooth health and development.

## RESULTS

We found that there were no differences in foods high in PUFAs between groups and there were no significant associations between PUFA intake during pregnancy and child tooth health and development. The greatest predictor of tooth maturation was maternal exercise level.

## CONCLUSION

Data from this study suggest maternal PA during pregnancy is a stronger influence of child oral health outcomes. All Healthcare providers seeing pregnant women should counsel them on the importance of PA during their pregnancy.

# GENOME SEQUENCING IDENTIFIES THE CAUSATIVE VARIANT IN AN UNEXPLAINED CASE OF NEONATAL MARFAN SYNDROME

**KATRI THIELE BS, MONICA H WOJCIK, MD, CARLY GRANT, MS, LGCG, JULIA GOODRICH, PHD, RONALD LACRO, MD, WEN-HAN TANN, BMBS, PANKAJ AGRAWAL, MBBS, MMSC**

---

## BACKGROUND

Neonatal Marfan syndrome is a rare connective tissue disease with a poor prognosis. The molecular basis underlying this early-onset form of Marfan syndrome is a de novo variant (often missense or intronic, resulting in exon skipping) within exons 24-40 of FBN1.

## METHODS

We describe a patient who presented with a phenotype highly consistent with Marfan syndrome at birth, including severe arachnodactyly, facial dysmorphism, and rapidly progressing aortic root dilation. The patient's preliminary molecular analyses failed to reveal a pathogenic variant in FBN1, posing the conundrum of a compelling clinical diagnosis that remained unsupported by molecular analysis.

## RESULTS

Six years postmortem, while exome sequencing was still unrevealing, genome sequencing revealed a deletion spanning part of exon 33 and the adjacent intron of FBN1 that had been missed on prior deletion/duplication analysis. This confirmed the diagnosis of neonatal Marfan syndrome. This patient's case emphasizes the utility of genome sequencing in detection of copy number variants, which contribute to >10% of Mendelian disease, yet are not reliably captured by more common next generation sequencing techniques.

## CONCLUSION

This highlights a class of variants that is difficult to detect by standard genetic testing approaches, and which should be considered in newborns with a presentation suspicious for genetic disease, but with inconclusive workup.

# TRANSORAL AND SUBMENTAL THYROIDECTOMY (TOAST): A HYBRID APPROACH TO SCARLESS THYROIDECTOMY

CHELSEA VISCARDI; YUFEI CHEN, MD; IHEOMA NWAOGU, MD; QUAN-YANG DUH, MD, INSOO SUH, MD

## BACKGROUND

Endoscopic approaches to thyroidectomy have been evolving to have reduced or non-existent scarring. The transoral endoscopic thyroidectomy vestibular approach (TOETVA) has been established as a feasible and safe option for select patients who desire no scar, but can result in post-operative pain along the center of the chin and capsular disruption of larger thyroid nodules. This prompted development of the hybrid approach transoral and submental thyroidectomy (TOaST). TOaST allows for minimal dissection of the chin and a larger space for removal of the specimen while maintaining favorable cosmetic outcomes. There is one case study of a 33-year-old female who had a successful excision of a 4.2cm follicular adenoma with no complications via TOaST.

## OBJECTIVE

The objective of this study is to establish feasibility of the TOaST procedure through a small case series.

## METHODS

Patients were recruited to the study who fit the criteria of a thyroid cancer <2cm in maximal dimension, benign thyroid nodule <6cm in maximal dimension, indeterminate thyroid nodule <4cm in maximal dimension, goiter from either Grave's disease or multinodular <6cm in maximal dimension. Exclusion criteria included prior head or neck surgery, trauma or irradiation, a BMI of >45, or higher risk features for thyroid nodules as seen on imaging. Each participant had the TOaST procedure performed by an endocrine surgeon at UCSF.

## RESULTS

Seven patients, 6 female and 1 male, with benign or malignant thyroid disease of one or both lobes were included in this study. The average age was 37.8 years old and average BMI was 23.94. The mean operative time was 157 minutes. The estimated blood loss was 7.14mL and average size of nodule removed was 2.25cm. There were two complications, and neither was permanent.

## CONCLUSION

This case series of seven patients indicates that TOaST is a technically feasible approach to thyroidectomy. There were no permanent complications seen in these initial surgeries, and the results were cosmetically favorable. To continue evaluating this technique, a larger case series will be conducted.

# **INFLUENCE OF HAVING A PRIMARY CARE PROVIDER ON ADMISSION FROM THE EMERGENCY DEPARTMENT**

**NIKI WINTERS B.S., NICK BRANDON M.D., JUHI GOR B.S., CASSANDRA BRADBY M.D., THEODORE DELBRIDGE M.D. M.P.H.**

---

## **BACKGROUND**

Over the past two decades, Emergency Department (ED) visits have been increasing at a rate faster than the healthcare system can keep up. The ED sees a variety of complaints ranging from those that need urgent medical attention to those that could be treated in a primary care setting.

## **OBJECTIVE**

The purpose of the study was to determine if a recent encounter with a Primary Care Provider (PCP) is associated with the likelihood of admission to the hospital from the Emergency Department (ED).

## **METHODS**

922 surveys were collected at Vidant Medical Center's Adult Emergency Department from May to July 2018. Patients with altered mental status, critically ill patients, and trauma patients were excluded from the study.

## **RESULTS**

Of the 922 surveys collected, approximately three-fourths (77%) reported having a PCP. Of the 261 patients who spoke with a doctor prior to their ED visit, 58% were told to come to the ED for evaluation and 67.6% of those people were subsequently admitted to the hospital from the ED. It was noted that those with insurance were more likely to have a PCP ( $p < 0.001$ ), these patients were also more likely to contact a doctor prior to their ED visit ( $p < 0.001$ ). In addition, those who saw a doctor within 48 hours of an ED were more likely to be admitted than those who have not seen a doctor within the past year (77.9% vs 35.6%).

## **CONCLUSION**

Having insurance was shown to be associated with a patient's likelihood of having a PCP. In addition, those patients who contacted their PCP prior to coming to the ED were more likely to get admitted than those who did not contact their PCP. This suggests that patients contacting their PCP prior to an ED visit could prevent unnecessary ED visits. Furthermore, patients that had more recently seen a doctor were more likely to be admitted to the hospital, suggesting medical issues that needed further medical attention.

# SPINAL CORD EPENDYMOMAS: VARIANTS AND TOPOGRAPHY SEEN AT A SINGLE INSTITUTION

NIKI T. WINTERS, B.S., JONATHAN D. DVORAK, M.D., K. STUART LEE, M.D., SHAWN M. COLLINS, B.S., REGIS HOPPENOT, M.D., HILAL KANAAN, M.D., WEN ZHONG, M.D, PHILIP J. BOYER, M.D., PH.D.

## BACKGROUND

Ependymomas are glial neoplasms which arise along ventricular surfaces in the cerebral hemispheres and posterior fossa and along the spinal canal of the spinal cord. Histopathologically, classic, papillary, clear cell, tanycytic, and myxopapillary variants of ependymoma are recognized and can be classified as grade I, II, or III (anaplastic) using World Health Organization (WHO) criteria. Myxopapillary ependymomas typically arise in an extraaxial location in association with the conus medullaris, cauda equina, or filum terminale and are WHO grade I lesions; other variants typically arise as intramedullary lesions and are grade II or III lesions.

## OBJECTIVE

Tanycytic ependymomas of the spinal cord are rare at our facility and in the literature.

## METHODS

A search of the East Carolina University Department of Pathology and Laboratory Medicine laboratory information system was conducted to identify all cases of ependymomas accessioned during the previous 30 years. Cases for which glass slides were available were reviewed and classified using 2016 WHO criteria and the site of occurrence was documented. A PubMed search was carried out using key words including ependymoma, myxopapillary, tanycytic, and spinal cord. Medical records for five representative spinal cord cases were reviewed and summarized.

## RESULTS

A total of 88 cases diagnosed as ependymomas have been treated neurosurgically at our center, 29 (33%) of which were identified as intramedullary or extramedullary lesions associated with the spinal cord. Spinal cord lesions have included classic (15), myxopapillary (14), and tanycytic (1) variants. Literature search revealed that approximately 50% of adult ependymomas occur in the spinal cord and the uncommon tanycytic ependymoma most often occurs as an intramedullary lesion. Our tanycytic ependymoma occurred in the conus medullaris and, to date, only six other extramedullary cases have been reported.

## CONCLUSION

In our series, approximately a third of ependymomas occurred within the spinal cord, a lower proportion than reported in the literature. Tanycytic ependymomas are uncommon and usually occur as intramedullary lesions within the spinal cord; six other extramedullary cases have been reported. Given their spindle cell phenotype and general absence of rosettes, they can be confused with both astrocytomas and Schwannomas.

# PROTON-SENSING GRP68 EXPRESSION DECREASES FOLLOWING ARTERIAL ISCHEMIC INJURY

MICHAEL WISNIEWSKI, JOSH MORGAN, JAKE FRANCISCO, MICHAEL BULLOCK, DR. NATHAN HOLLAND, DR. DAVID TULIS

## BACKGROUND

Cardiovascular disease (CVD) remains a leading cause of death in the United States and in the world. Foundational to the pathogenesis of CVD are vessel damage and dysfunction, specifically abnormal vascular smooth muscle proliferation. In addition, the local acidotic microenvironment caused by reduced blood flow to surrounding tissue exacerbates vessel dysfunction. Common to VSM cells is GPR68, a proton-sensing G protein coupled receptor. GPR68 is fully activated at a pH of 6.8, suggesting it may sense the acidotic microenvironment associated with CVD and contribute to pathogenesis.

## OBJECTIVE

We hypothesized that vessel injury and the ensuing acidosis would increase GPR68 expression within vascular smooth muscle.

## METHODS

C57Bl/6J wild type mice were subjected to vascular injury via a left common carotid artery (LCA) ligation surgery. Mice were anesthetized and the LCA was ligated just proximal to the bifurcation of internal and external branches to induce injury and localized acidosis. Twenty four hours post-surgery, mice were euthanized and the LCAs and right common carotid arteries (RCAs) were harvested and snap frozen. For control tissues, uninjured mice were euthanized and tissues harvested in the same fashion. Later, vessels were homogenized, protein levels were quantified with a Bradford assay, and subsequently probed for GPR68 using western blotting. Blots were analyzed for densitometry and data was subjected to Student's T Test and 2 way ANOVA with post hoc Tukey Tests. A p-value < 0.05 was deemed significant.

## RESULTS

GPR68 expression was not increased in the injured LCAs. However, there was a statistically significant decrease in GPR68 expression in the injured LCAs compared to the uninjured LCAs (p value = .0018). Sex of the animal did not impact GPR68 expression. For control, there was no difference in GPR68 expression in the RCAs of uninjured animals compared to the RCAs harvested from animals with injured vasculature (p value =0.16).

## CONCLUSION

GPR68 expression decreases in the setting of acute injury/acidosis. Basal GPR68 activity in normal VSM may serve a protective role and the absence of GPR68 following injury may contribute to CVD pathogenesis.



# OPTIMIZING THE DOSE OF SBRT/CKRS RADIATION IN PATIENTS WITH METASTATIC CANCER BEING TREATED WITH IMMUNOMODULATING DRUGS

SUSAN WOODY, MS2, MS, PHARMD; APARNA HEGDE, MD; HYDER ARASTU, MD; MARK BOWLING, MD; NITIKA SHARMA, MD; PAUL WALKER, MD AND ANDREW JU, MD

---

## BACKGROUND

Increasing antigen production via localized radiation to enhance the immune system's ability to detect and destroy cancer outside of the irradiated region is termed the abscopal effect. Recently, there has been an increased interest in the abscopal effect due to the introduction of immunomodulating drugs. Specifically, it is thought that combining the abscopal effect with immunomodulating drugs meant to increase the immune system's effectiveness, such as nivolumab, could improve outcomes in metastatic disease.

## OBJECTIVE

While this is a newer strategy for treating metastatic disease, there are still a lot of unknowns on how to maximize therapy effectiveness. In this study, our goal is to examine how the dose of radiation from SBRT/CKRS impacts a patient's response if they were also treated with immunomodulating drugs. A dose of radiation too low may not produce the antigens necessary for an abscopal effect, and individual doses at or above 1200-1800 cGy have been shown in molecular studies to degrade cytosolic DNA, thus potentially dampening the immune response.<sup>1</sup>

## METHODS

In order to answer this question we have undertaken a retrospective analysis of patients treated with SBRT/CKRS and immunomodulating therapy at Vidant Medical Center since 2014. We included all NSCLC patients receiving SBRT/CKRS to various body locations, and those without NSCLC that were treated with SBRT/CKRS to the lung. In addition, patients needed to have received immunomodulating therapy. Currently, we have identified 65 patients that have been treated with immunomodulating therapy and SBRT/CKRS since 2014. Due to patients often having multiple sites of treatments with SBRT/CKRS, we have identified at least 160 lesions that have been treated. From here we have begun tracking the individual lesion outcome, time to metastasis, and overall response.

## CONCLUSION

Using this information, we expect to find that there will be an optimal dose of radiation that will produce the best response when given in conjunction with immunomodulating drugs.

# **SUBEPIDERMAL BLISTERING INDUCED BY IGA AUTOANTIBODIES TO BP180 IS MEDIATED BY HUMAN FCA RECEPTORS IN A HUMANIZED LABD MOUSE MODEL.**

**J. YANIK BSN, AND Z. LIU PH.D.**

---

## **BACKGROUND**

Linear IgA bullous dermatosis (LABD) is an autoimmune blistering disease of the skin mediated by IgA autoantibodies against the basement membrane zone (BMZ) protein BP180 at the non-collagenous 16A (hNC16A) region. There is no immune cross reactivity between hNC16A and the corresponding mouse domain, requiring a humanized hNC16A mouse model to study LABD in vivo. The exact mechanism of LABD IgA autoantibodies in disease pathogenesis remains largely unknown and the pathogenicity of IgA autoantibodies from LABD patients has never been demonstrated. The purpose of this study is to create a mouse model to study the cellular and molecular mechanisms underlying LABD. We hypothesize that anti-hNC16A IgA autoantibodies in LABD induce subepidermal blisters via IgA receptor (FcαR1)-dependent activation of PMNs.

## **METHODS**

hNC16A-specific total IgA was purified from patient sera collected from two patients with active LABD. Purified IgA from normal human subjects were used as control. Immune activity against NC16A in LABD was detected by immunoblotting using recombinant NC16A and by indirect immunofluorescence using hNC16A mouse skin sections. Neonatal hNC16A mice received hNC16A-specific IgA or control IgA via intradermal injection. The antibody injected mice were examined 0-48 hours after injection. After clinical examination the animals were killed and skin samples were obtained. The skin sections were examined by direct immunofluorescence and routine histology staining. hNC16A mice were injected with human PMNs or mouse PMNs ( $1 \times 10^6$  PMNs/mouse) and 30 minutes later injected intraperitoneally with control IgA or anti-NC16A IgA and examined 48 hours later as described above.

## **RESULTS**

LABD IgA recognized recombinant hNC16A in in vitro and in vivo studies. Passive transfer of anti-hNC16A IgA and not control IgA, deposits in the BMZ in neonatal hNC16A mice by DIF, but does not induce LABD clinically. Only mice reconstituted with hFcαR1-expressing PMNs and injected with anti-hNC16A IgA developed LABD.

## **CONCLUSION**

This is the first in vivo demonstration that LABD IgA autoantibodies are pathogenic. Human PMNs are required for experimental LABD in single humanized hNC16A mice. There is no murine IgA receptor (FcαRI) for human IgA. For in vivo experiments, the reconstitution of mice with human to hFcαRI-expressing PMNs provided a necessary step for the induction of disease pathology. A new LABD animal model, double-humanized hFcαR1/hNC16A mouse, will be useful for study of disease mechanisms and development of new therapeutic strategies.

# USING FLUORESCENTLY TAGGED A-SYNUCLEIN TO MONITOR TG2 MACROMOLECULAR ASSEMBLY: DETERMINING BIOPHYSICAL PROPERTIES THAT PROMOTE LEWY BODY AMYLOIDOSIS

**B. A. ZECHES, J. WASHINGTON, A. H. DESANTIS, A. HONDROS, T. N. ZECZYCKI**

## BACKGROUND

Parkinson's disease (PD) is characterized by dopaminergic-neuronal cell death within the substantia nigra pars compacta. In addition to progressive neurodegeneration within mesencephalic nuclei, PD is histopathologically marked by cytoplasmic proteinaceous intraneuronal inclusions, termed Lewy bodies. These inclusions largely contain aggregated,  $\alpha$ -synuclein amyloids. Formation of these aggregates can be exacerbated by the  $\text{Ca}^{2+}$ -dependent activity of transglutaminase 2 (TG2) via enzymatic crosslinking. This acyl-transfer reaction generates products highly resistant to homeostatic autophagy and ubiquitination, promoting amyloidosis in PD and other  $\alpha$ -synucleinopathies including Alzheimer's Dementia and Huntington's Chorea.

Although TG2 is universally expressed in human tissue, the mechanisms underlying its molecular interactions are poorly understood. TG2 possesses intrinsically disordered binding regions that lend itself to multiple substrate interactions which include amyloid  $\beta$  A4 peptide, tau, and huntingin outside of  $\alpha$ -synuclein. Prevention of TG2:substrate interactions by small molecular inhibitors may offer a viable option for therapeutics designed to slow the progression of disease. Thereby, we need to understand the molecular mechanisms governing the protein-protein interactions and macromolecule assembly of TG2 and its substrates.

## OBJECTIVE

To determine the energetics of TG2 and  $\alpha$ -synuclein macromolecular complex as a function of temperature using fluorescently tagged  $\alpha$ -synuclein (N- (G7C) and C- (A91C) terminal) to monitor TG2- $\alpha$ -synuclein interactions.

## METHODS

Decreases in relative fluorescence of tagged  $\alpha$ -synuclein (i.e. pyrene, acrylodan, and BADAN) were monitored at equilibrium at varying TG2 concentrations and temperatures. Surface plasmon resonance (SPR) was used to compare the binding affinities of the reporter probes of labeled  $\alpha$ -synuclein to the WT.

## RESULTS

Site-directed mutagenesis of  $\alpha$ -synuclein successfully facilitated thiol-reactive probing. Qualitative analysis of mutants, G7C and A91C, show decreased and insignificant change in fluorescent detection respectively. SPR analysis of WT and G7C  $\alpha$ -synuclein yielded the following association constants:

$\alpha$ -synuclein	ka1 [1/(M*s)]	kd1 [1/s]	KD1 [M]	ka2 [1/(M*s)]	kd2 [1/s]	KD2 [M]
WT	1.81e3	1.26e-3	6.97e-7	9.50e1	3.72e-14	3.92e-16
G7C	2.19e3	5.07e-3	2.31e-6	2.26e2	1.32e-3	5.83e-6

## CONCLUSION

Fluorescent quenching of G7C mutants indicate that the N-terminus of  $\alpha$ -synuclein may be interacting with TG2, playing a role in complex stability. A91C mutants did not observe any significant fluorescent decrease with TG2 titration demonstrating that the C-terminus is inconsequential during binding.

# THE EFFECT OF SLEEP DISORDERED BREATHING ON COGNITIVE FUNCTION IN PATIENTS WITH NORMAL PRESSURE HYDROCEPHALUS

CONNIE S ZHONG, ALEXANDER DAVIS, ARUNA RAO

---

## BACKGROUND

Both normal pressure hydrocephalus (NPH) and sleep apnea (SA) are associated with cognitive deficits. The former specifically in executive function, memory and attention domains. We wanted to explore the specific cognitive domains affected in NPH patients with and without SA.

## OBJECTIVE

Patients with both NPH and SA have lower scores in attention, memory and recall domains of the Montreal Cognitive Assessment (MoCA) test.

## METHODS

A retrospective chart review of patients with presumed NPH who were admitted to The Johns Hopkins Hospital between the years 2016 and 2018 for extended lumbar drainage (ELD). All patients were administered the MoCA and 33 obtained polysomnograms.

## RESULTS

Analysis was performed using STATA 15.1. Independent variable was SA and dependent variable was individual MoCA domain scores. Covariates include demographic and anthropometric measurements. In our sample 52.7% were male, 83.3% white. 26 (73.3 %) had polysomnograms. 69.2% had SA (apnea hypopnea index of more than 5 per hour).

We used unpaired t-tests to analyze differences in MoCA scores in patients with and without SA. Visual spatial  $p=0.22$ , Naming  $p=0.35$ , Attention  $p=0.41$ , Language  $p=0.49$ , Abstraction  $p=0.28$ , Recall  $p=0.88$ , Orientation  $p=0.79$ .

## CONCLUSION

In patients with NPH, there was no statistically significant difference in MoCA scores in those with sleep apnea.

Our results suggest that sleep apnea does not affect cognition in patients with NPH.